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EDITORIAL

THE ETHICS OF MULTIPLE SEIZURE

"Diseases desperate grown
By desperate appliances are relieved
Or not at all."

SHAKESPERE, however, was anticipated by Hippocrates who said that "Extreme remedies are very appropriate for extreme diseases."

"Multiple seizure" is the term applied by the authorities charged with enforcement of the Federal Food and Drug acts, by which samples of suspected products are purchased simultaneously at several points and suits brought promptly at each point. This, of course, involves much greater expense to the marketers of such products than if only one purchase should be made. Complaint has been made by some persons and some organizations about this practice and the authorities have deemed it advisable to publish some facts in regard to the matter. It is pointed out that in many cases if only a single sample is libeled, the docket of the court in that locality may be so overloaded that months may elapse before a trial can be had, thus embarrassing both prosecutor and defendant. In further defense of the practice, the department has set forth in detail the character of some of the articles that have been seized under this system, and it is shown that they represent a most appalling array of fraudulent claims. The number of cases of multiple seizure is not large. From July 1, 1924, to October 1, 1929, about two score instances are enumerated, some of which have not yet been brought to court decision.

As an evidence that sale of this class of products is one of the most flagrant types of fraud, the following descriptions are taken from the department pamphlet. Full names and addresses of the manufacturers are given in the pamphlet, but these data are not necessary here.

A Germicide and Blood-Purifier, camphor and ether dissolved in linseed oil possessed neither germicidal nor antiseptic properties. In addition to the unwarranted name, the label presented the preparation as a treatment for rheumatism, asthma, catarrh, throat troubles, blood and skin diseases, diseases of the stomach and bowels, and ailments of an inflammatory nature, either internal or external. It was stated that the preparation would remove the cause of nearly all diseases. Consumption, pneumonia, la grippe, pleurisy, paralysis, syphilitic affections, and prostatic troubles were mentioned on the labeling.

Compounds Nos. 1 and 2. Both of these articles consisted of sodium and calcium borate, nitrate, and sulphate, extracts of licorice and uva ursi, a laxative drug and salicylic acid, with alcohol 5 per cent. and water 90 per cent. No. 1 was offered for Bright's disease and No. 2 for diabetes.

Preparations recommended for psoriasis and chronic, stubborn eczema of all kinds. There were three of these, designated at No. 1, No. 2, and No. 3. They all contained chrysarobin, and in addition No. 1 contained ether, alcohol and water, and No. 2 and No. 3 contained resorcin, salicylic acid, glycerol, volatile oils, alcohol, and water.

An ointment, consisting essentially of a mixture of fat and petrolatum in which was incorporated zinc oxide and traces of menthol and thymol was recommended not only for eczema, scrofulas, and boils, but also for diphtheritic throat, pneumonia, scarlet fever and smallpox.

Spirit of niter, spirit of camphor, and similar preparations were found to contain isopropyl alcohol, which is forbidden by the U. S. Pharmacopœia, the addition being made solely for saving money in the manufacture.

A preparation especially intended for babies was found to contain morphine sulphate. It was recommended for free use to very young infants. Its sale was, of course, in violation of the Harrison act as well as of the general food and drug act.

A preparation composed mainly of Epsom salt in water with small amounts of other ingredients including iron, quinine and strychnine salts was colored red with a coal-tar dye and labeled as a blood builder, and blood purifier. A 32-page booklet accompanying the package consisted almost entirely of fraudulent representations regarding the effects of the preparation. In the booklet were numerous

testimonials setting forth the virtues of the article for a wide variety of diseases, including boils and carbuncles, eczema, flu, high blood pressure, neuritis, pyorrhea, rheumatism, nervous prostration, etc. Other testimonials related to the effect of the preparation in increasing weight and improving physical appearance.

A mixture, essentially phosphate, glycerol and water with a small amount of some vegetable extract, and colored with a red dye, was represented as a remedy for high blood pressure.

An injection, Rx 500, was a water-solution of boric acid and zinc sulphate colored with a yellow dye. The label said "scientific remedy for all stages of membrane inflammation." "Will stop pus formation in two or three days. A boon to suffering manhood."

Henry Leffmann.

SELECTED EDITORIAL

THE ETHER PROBLEM*

KNOWING the vigilance exercised generally by the manufacturers of anesthetic ether, it has been something of a shock to note from time to time the seizures made because of failure to meet the requirements of the United States Pharmacopœia, and to learn that for years patients have developed respiratory complications, and in some instances pneumonia, following surgical operations. Surgeons and anesthetists generally have relied upon the standard brands and trade-marks of ether, because of the continuous research conducted by manufacturers striving not only for absolute purity of the product but also for a better understanding of factors important in its preservation. Concurrently, the federal laboratories have kept in the closest touch with the problem, and it has been our privilege to publish data dealing with progress made in its solution.

In one hospital a chemist particularly well fitted to undertake the task was asked to consider possible causes of post-operation bronchitis and pneumonia. He raised the question of ether purity and was told that it was all right, being of a standard brand. He nevertheless examined it and found considerable quantities of both peroxide and aldehyde, which are interdicted by the Pharmacopœia, and both of which render ether unfit for anesthetic purposes. Experi-

*Reprinted from *Industr. and Engineering Chemistry.*

ments were undertaken, jointly with a pharmacologist, using the oyster as the initial experimental animal since it has the same type of structure as the respiratory tract lined with cilia which eject foreign bodies upward from the tract. By using cold light through a quartz rod it was possible to study the effect of ether upon the ciliary action in the oyster. It was found that, whereas pure ether was without effect upon movement, 0.001 per cent. of acetaldehyde would entirely stop ciliary action. Unfortunately, ether is not a stable product. Some oxidation takes place, in part perhaps as a result of contact with the catalytic system of metal, water, oxygen, and ether. This has led to many efforts on the part of manufacturers to provide better containers. Carbon dioxide has been used to expel the air, copper-plated cans and various other types of containers or chemical treatment of such containers have been introduced in an effort to improve ether preservation. In five European countries the law requires anesthetic ether to be packed in amber glass, in which some claim it will remain in a state of purity for a long time. If it can be demonstrated that the packaging of ether in this manner will prevent deterioration for a measurable length of time so that dates would afford reasonable protection, it would be worth many times the additional cost and any inconvenience in transportation which might be involved. The effort to provide antioxidants should go forward and, should this prove the solution, our surgeons would soon become educated to the use of permissible preservatives, although now they object to color and to the presence of residual matter when the ether has evaporated.

It should be emphasized that reputable manufacturers are honestly trying to prevent other than the best material reaching the operating rooms. It must also be said that the federal laboratories and inspectors are checking ether and to the best of their ability rounding up and withdrawing from the market or from use material which has deteriorated in storage. The manufacturers are doing all they can to prevent the spoilage of their ether after it has left their inspectors. It is not our purpose to censure anyone nor to criticize what has been done. We do consider the problem a pressing one, and wish to emphasize the opportunity for service presented to the chemical profession to attack it in the belief that sustained effort will bring a solution. In the meantime we particularly urge hospitals to detail a competent chemist to stand guard over their ether supply, not when it is purchased, but when it is about to be used, that impure material may not contribute to the loss of a single life.

ORIGINAL ARTICLES

FUMIGATION WITH FORMALDEHYDE

By David Wilbur Horn and Arthur Osol [1]

FUMIGATION SEEMS frequently to be conceived by others just as it is pictured for them by a few. This seems more or less usual in connection with practices that have had their origin in superstition. In such conceptions features of merit may or may not be present, and upon this science, and not authority, is the arbiter. "There are indeed two things," according to Hippocrates, "knowledge and opinion; of which the one makes its possessor really to know, the other to be ignorant."

Points of view essential to a sensible and satisfactory handling of terminal fumigations, have remained entirely unused. Obvious suggestions of a proper approach have been ignored. New methods and, more particularly, unauthorized modifications of older methods, have been ushered into the literature without due knowledge and without caution as to the relative magnitudes of yields or of costs. It is astounding to find men lending their names so easily to processes poorly conceived, to procedures of doubtful merit, and to general remarks worthy of children. "It is an indignity to common sense to contemplate accepting as reliable all that has been written about the efficacy of the methods (of fumigation). . . . One must conclude either that a good many people have written convincingly about these matters when they knew very little about them, or else that a highly variable experimental procedure has been used to determine the effectiveness of these several methods. . . ." [2] "There is no doubt that the lack of uniform methods of application under fixed conditions is responsible in a very great measure for the discredit into which disinfection has fallen with a large percentage of professional men." [3]

The time has long since arrived when men should put terminal

[1] Many of the experimental results in this paper are from work submitted by Arthur Osol to the Philadelphia College of Pharmacy and Science in partial fulfillment of the requirements for the degree of M. Sc.

[2] Horn, *Proceedings of Delaware County Institute of Science,* June, 1920, p. 51, "Fumigation with Formaldehyde." This monograph is obtainable from the Secretary, at Media, Pennsylvania.

[3] Dreyfus, *J. Amer. Pub. H. Assoc., IV,* p. 1046, 1914.

fumigation upon a scientific basis, or should frankly confess to ignorance and indifference and for these poor reasons agree arbitrarily to throw terminal fumigation officially into the discard.

In this paper the primary object is to furnish needed information regarding the yield of formaldehyde as gas in each of a number of methods of fumigation. However, the general problem of terminal fumigation is re-stated and discussed, with the intention of provoking in the reader rational mental processes upon this matter. Only the methods in which formaldehyde is vaporized from formalin [4] by the heat of oxidation or of dehydration will be taken up. Water vapor is as essential as formaldehyde for bactericidal efficiency, and these methods involving chemical actions seem to include all the methods that may yield a high concentration of formaldehyde and of water vapor promptly and that are at the same time practical for routine use by health officers and free from fire risk. Exception to this statement may possibly be taken by those who think health officers may as readily fumigate with bed sheets hung up wet with formalin, or spend time atomizing formalin. We have not met health officers who care for either of these procedures.

Comparison of Different Methods of Fumigation

In comparing different fumigation mixtures, there are several ideas to be distinguished clearly from each other. One is the ratio of oxidizing or dehydrating agent to the formalin used; this we call the *mixing ratio*. Another is the ratio of formalin used to the cubic content of the room to be fumigated; this we call the *formalin dosage*. We state the *mixing ratio* in grams of reagent per 500 cc. of formalin, and the *formalin dosage* in cubic centimeters of formalin taken per 1000 cubic feet of room. It must be generally known that all of the formaldehyde in the formalin used is never evolved as gas, for some of it is always lost in chemical action; that percentage of the total that is actually evolved as formaldehyde gas in any method we call the *chemical efficiency* of that method. The *chemical efficiency* is apparently always a function of the *mixing ratio;* one cannot vary the *mixing ratio* without therewith altering the *chemical efficiency.* The accompanying data [5] (Table I) and graph (Figure 1) show the rela-

[4] Throughout this paper the word *formalin* is used to indicate the U. S. P. solution of formaldehyde; the word *formaldehyde* is used to indicate the compound CH_2O, so-called "absolute formaldehyde."

[5] Horn, *loc. cit.*, p. 47.

tion between mixing ratio and chemical efficiency for bleach and formalin. The mixing ratios are plotted as abscissae and the chemical efficiencies as ordinates.

TABLE I

Mixing Ratios and Chemical Efficiencies in Bleach-Formalin Procedure

Mixing Ratio	Chemical Efficiencies
100 gr.	10.5%
200	15.1
250	19.1
500	27.2
750	29.6
1000	42.0

DEPENDENCE OF CHEMICAL EFFICIENCY UPON MIXING RATIO.

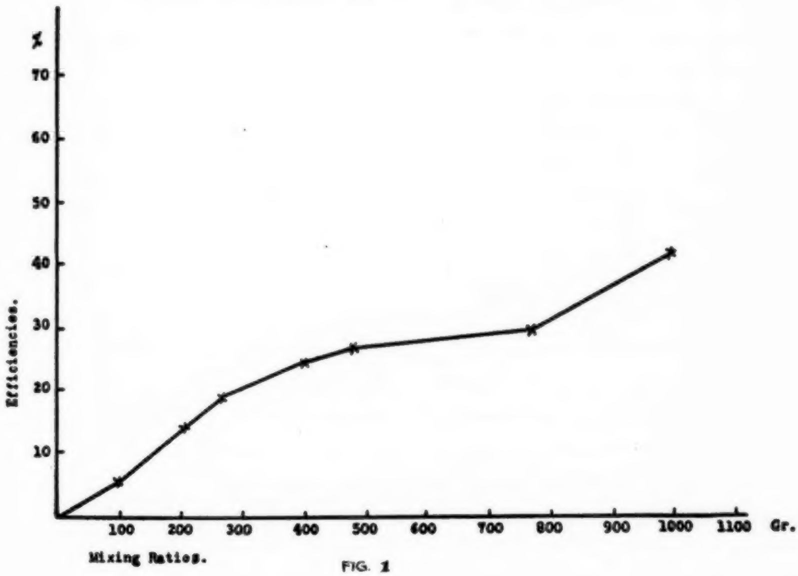


FIG. 1

Horn's analytical method [6] enables one to learn in any case the numerical value of the chemical efficiency. This figure along with the formalin dosage enables one to calculate the maximum concentra-

[6] Given in detail later in this paper; see p.

tion of formaldehyde attainable in the air of any room by following the directions for fumigation as given by any author. This maximum concentration we hereafter refer to simply as *the concentration;* and we state it as percentage by volume, i. e., as the decimal fraction of a cubic foot of formaldehyde per 100 cubic feet of room space. The maximum concentration attainable is given in the following table (Table II) for each method of record.

TABLE II

Concentrations of Formaldehyde Attainable by Following Different Authorities

Authority [8]	Concentration
Storm	0.30%
McClintic	0.21
Horn	0.21
Evans & Russell II	0.20
Evans & Russell I	0.17
Pozen & Dieter	0.13
Hasseltine	0.12
Park II	0.12
Crandall	0.10
Rosenau	0.10
Dixon	0.07
Park I	0.07
Park III	0.07
Park IV	0.05
Walker	0.03

It must certainly be admitted after study of Table II that there exists an utter lack of agreement among the several proponents of methods and of modifications of methods of fumigation, as to what is *the proper* (or lethal) concentration of formaldehyde to attain in a space that is being fumigated. It is a fact that even the idea of a proper concentration is not to be found in most of the writings on fumigations.

Certain things have to be known in order to be able to produce at will any desired per cent. of formaldehyde in a given air space, and these things have not been known to the proponents of most methods. Thus, it is absolutely essential to know in advance the chemical efficiency of the given mixture throughout a wide range of mixing

ratios. But in ignorance of this, each proponent has selected his mixing ratio for some irrelevant reason, such as "dry residue," "brisk evolution of gas," "gratifying results," etc., and has urged a formalin dosage that seemed to him proper for reasons that he seldom discloses. It requires only common sense to see how easily terminal fumigation as a public health measure may thus be reduced to an idle gesture.

Similarly, the matter of the relative costs of different procedures has been obscured by the same lack of definite knowledge. Mixing ratios, chemical efficiencies, and formalin dosages enter here as essential data side by side with market price of the chemicals used. To arrive at the relative costs of fumigation by different methods, one is compelled to select some fixed figure for the lethal concentration of formaldehyde (say, 0.21 per cent. by volume) just as one is compelled to select some fixed figure (say, 1000 cubic feet) for the space to be fumigated. There is to date no recognized, or suggested, lethal concentration of formaldehyde, for fumigations seem not to have been thought of in just this way. We think this need should finally be met and supplied by consensus of well founded opinions—as by some suitable committee on standards. For calculating the relative costs of the several methods we have taken tentatively as the basis of lethal concentration of 0.21 per cent. by volume. This is practically the concentration attainable in the oldest official American method. This concentration was decided upon by the State of Maine proceeding rationally upon the basis of extended experiments of skillful men, and with conscious endeavor to allow a needed factor of safety. Substantially this concentration was later independently recommended by McClintic of the U. S. Public Health Service; McClintic's concentration differs from that of the State of Maine by only .01 per cent. This concentration is the highest in American procedures, although Werner [15] upon the basis of a careful study calls for about twice as much as this as a minimum. Using a volume per cent. of 0.21, and the market prices of July, 1929,[7] we have calculated and give in the following table (Table III) the costs of one fumigation of 1000 cubic feet by the several processes that we are dealing with in this paper.

[7] *J. Ind. and Eng. Chemistry*, XXI, p. 803, Aug., 1929.

TABLE III

Costs of Fumigating 1000 Cubic Feet

Method[8]	Cost
Storm	9¢
McClintic	20
Evans & Russell II	21
Hasseltine	21
Park II	21
Pozen & Dieter	21
Horn	21
Evans & Russell I	22
Rosenau	23
Park I	24
Park III	26
Park IV	36
Walker	37
Dixon	44
Crandall	63

This table shows how important is the consideration of relative costs. Since Crandall's method costs seven times as much as Storm's, one would naturally look for some great advantage involved to offset such a great disadvantage in cost. Again, why should Rosenau modify Horn's method when Rosenau's modification involves an increase of nearly 10 per cent. in cost? Why should Park give, without remark, alternative methods one of which is eight-sevenths as costly as the other? And why should Park say without warning that "a saturated solution of aluminum sulphate may be used instead of concentrated sulphuric acid" when actually this substitution raises the cost from 26 cents to 36 cents per 1000 cubic feet fumigated? These are examples of the pertinent questions that arise when costs are considered.

[8] Evans & Russell I refers to their method where 187.5 gr. $KMnO_4$ were used. Evans & Russell II refers to their method where 237.5 gr. $KMnO_4$ were used. Park I refers to Park's method where $KMnO_4$, formalin, lime and oxalic acid are directed. Park II refers to Park's method where $KMnO_4$, formalin and lime are directed. Park III refers to Park's method where lime, formalin and sulphuric acid are directed. Park IV refers to Park's method where lime, formalin and alum are directed. See Evans & Russell, 13th and 14th Report, State Board of Health of Maine. See Park, "Public Health and Hygiene," 2d Ed., 1928, Philadelphia.

When we confine consideration strictly to some one procedure, as for example to the action of permanganate upon formalin, without regard to sponsors, a most important relationship is found to exist between the cost per 1000 cubic feet and the mixing ratio used. This is because the chemical efficiency is a function of the mixing ratio. The following data [9] (Table IV) and graph (Figure 2) show for permanganate-formalin the dependence of the cost, upon the mixing ratio that may be adopted.

TABLE IV

Permanganate-Formalin Procedure
The Variation of Cost with Mixing Ratio

Mixing Ratio	Cost per 1000 cu. ft.
100	53¢
150	28
187.5	22
237	21
250	20
500	21
730	25
1000	25

DEPENDENCE OF COST UPON MIXING RATIO.

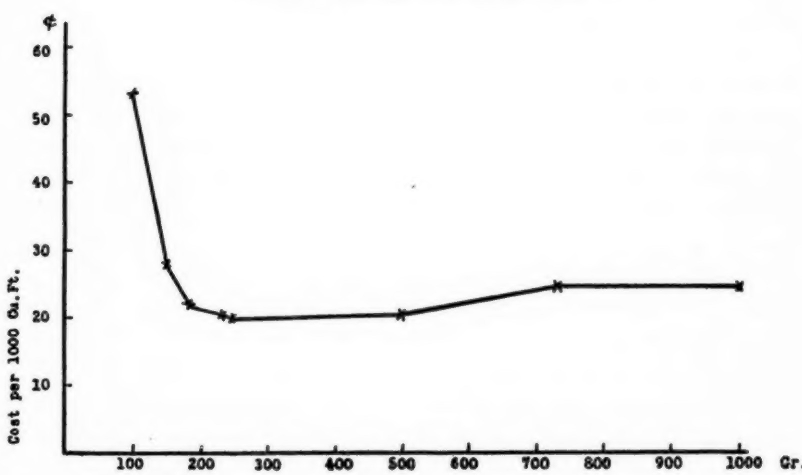


FIG. 2

[9] Horn, *loc. cit.*, p. 38.

The existence of a minimum cost could scarcely be guessed by any one, but when the data are assembled, particularly in the form of a graph, it becomes very evident. Without such consideration as this, rational selection of a proper mixing ratio is impossible. Of course it does not follow that the corresponding graphs for other chemical agents than permanganate will have the same form but it is unquestionably true that there is some such graph for each chemical agent and that such consideration is necessary before rational selection of the best mixing ratio can become possible. With the exception of the bleach-formalin procedure, such consideration does not appear and is not suggested, anywhere in the literature.

The Germicidal Effect

It will be admitted on all sides that when the matter of fumigations is thoroughly understood, if ever, it should become possible to formulate some equation including all the factors determining the germicidal effect. We suggest it may be some such equation as this:

$$g = k. \frac{c.F.h.t}{r}$$

where

g, represents the germicidal effect of the process
c, the concentration of formaldehyde in the room
F, the temperature Fahrenheit
h, the relative humidity
t, the time
r, the resistance of the virus or pathogen, and
k, a constant of proportionality the numerical value of which will depend upon the units used in expressing the variables. For simplicity merely, we have taken each variable in the first power; perhaps some of the variables, for example *c* or *r*, enter as higher powers or as exponents.

To anyone fairly familiar with fumigations, this succinct statement will suggest at once the discouragingly small amount of *knowledge* available to day in this subject.

The conventional bacteriological procedures have repeatedly demonstrated the potential effectiveness of fumigations. Thus among the earlier bacteriological work on fumigations by methods dealt with in this paper we may cite Russell's work with upward of 1500 cultures on the Evans permanganate-formalin method, and McClintic's work on Base's modification of Evans method. But it must constantly

be remembered that these satisfactory results were all dependent upon a satisfactory but more or less fortuitous combination of all the circumstances suggested by the symbols on the right-hand side of the equation just given. This feature of chance in the successful methods has been overlooked by many, and new methods and modifications have been brought forward with poorer luck and without regard to whether or not the conditions necessary for germicidal action were probably met.

The Concentration of the Formaldehyde

This is the most obvious of the determining factors in the success of a fumigation. In going over the literature, it is soon evident that nearly all proponents of new procedures in fumigation (See Table II) have offered nothing but qualitative evidence of the evolution of sufficient formaldehyde to justify their suggestions. The true reason for this is that the quantitative determination of the formaldehyde evolved was not an easy problem in quantitative analysis. Von Brunn (1899), and Base (1906), succeeded in the quantitative analyses of the air of rooms, for formaldehyde; and Horn (1917) developed a satisfactory quantitative laboratory procedure [10] for determining the formaldehyde evolved from fumigation mixtures. This method of Horn's for laboratory assay is very simple and checks closely with Base's results in his "zinc-lined room,"—using both the permanganate-formalin fumigation mixture, and lime-alum-formalin mixture.

In the following sections we shall take up the yields by several methods, particularly those found in the authoritative and recently revised text books on Hygiene and Preventive Medicine by William H. Park and by Milton G. Rosenau.[11] But before doing this, we shall first give an adequate discussion of the method of assay we have used.

Analytic Procedure

The apparatus (See Figure 3) is made from a round battery jar J (internal diameter 4 inches, depth 5 inches), and a tubulated bell jar B (internal diameter 3 inches, height 6 inches), serving together as a glass gasometer. A cylinder of glass C open at both ends (diam-

[10] *Loc. cit.*, p. 31.

[11] Park, "Public Health," 2d Ed., 1928, Philadelphia. Rosenau, "Preventive Medicine and Hygiene," 5th Ed., 1928, New York.

eter $1\frac{3}{4}$ inches, height $3\frac{3}{4}$ inches) supports a crystallizing dish D (diameter $2\frac{1}{4}$ inches, height $1\frac{1}{2}$ inches) or glass evaporating dish, in which the reaction occurs.

Approximately 500 cc. of distilled water are placed in the battery jar, and the glass cylinder set in position. The oxidizing agent in weighed amount is placed in D, and the measured volume of formalin is delivered upon it from a suitable pipette inserted through the

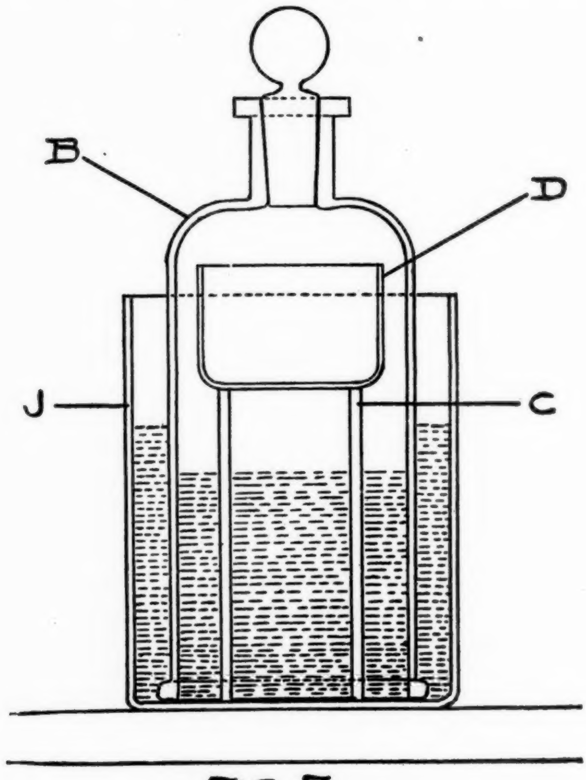


FIG. 3

tubulus of the bell jar. A jet of water should be used to moisten the ground surface of the tubulus before introducing the pipette. The pipette is rapidly withdrawn and the glass stopper immediately inserted into the tubulus. Although the expansion of the enclosed air combined with the hot gases evolved causes the bell jar to float up on the water, it is easy to adjust the charge and the volume of absorption water so as to avoid all loss of gas.

In devising and using such apparatus for fumigation assays, it is imperative to minimize the volume of water used for absorption. The reactions are so violent that small charges must be used, and unless the water is minimized the solution finally analyzed may be very dilute.

After the desired length of time the stopper is removed and rinsed with a jet of water; the bell jar rinsed in place in its inner surface with a jet of water, then raised from the water in the battery jar and rinsed, and finally stoppered and twice rinsed with water. The water in the battery jar is combined with the rinsings and diluted to a fixed volume in a measuring flask and then thoroughly mixed. In our experiments, the fixed volume was 600 cc. At this time and for comparison, a volume of formalin equal to that used in the experiment is delivered from the same pipette into water in another measuring vessel of the same size as that used above for the rinsings, and diluted to the mark.

The Volhard-Romijn method was applied to the absorption-water in the simplest possible way, so as to minimize both calculations and exact standardizations. The reactions represented by the following equations underlie our analyses:

$$(1)\quad H.C\begin{cases}H\\O\end{cases} + .HCN = H.C\begin{cases}H\\OH\\CN\end{cases}$$

$$(2)\quad HCN + AgNO_3 = AgCN + HNO_3$$

$$(3)\quad AgNO_3 + KSCN = AgSCN + KNO_3$$

The actual analysis of the absorption-water is conducted as in Table XI, using three volumetric flasks of 100 cc. capacity, designated as A, B and C. The chemicals are introduced into these flasks in the order and in the quantities indicated.

TABLE XI

Volumetric Flasks,	A	B	C
Potassium cyanide solution,	10 cc.	10 cc.	10 cc.
	50 cc. distilled water	50 cc. diluted formalin solution made for comparison	50 cc. absorption-water from fumigation experiment
C. P. conc. nitric acid,	4 cc.	4 cc.	4 cc.
Silver nitrate solution,	15 cc.	15 cc.	15 cc.
Distilled water, quantity sufficient for	100 cc.	100 cc.	100 cc.

The contents of the flasks are shaken and filtered through dry papers in funnels set in 100 cc. measuring cylinders. The first 20 cc. of each filtrate are discarded. 25 cc. of each filtrate withdrawn by a pipette to a 100 cc. beaker, 5 cc. of ferric alum indicator solution added and then 25 cc. of distilled water. The contents of each beaker are then titrated with potassium sulphocyanate solution.

If in one analysis for example there is required, of sulphocyanate solution, for flasks, A B C

1.50 cc. 2.92 cc. 2.03 cc. respectively,

it is clear that

(2.03 cc.—1.50 cc.) : (2.92 cc.—1.50 cc.) = x : 100%

In this particular case, x = 37.3 per cent., which means that 37.3 per cent. of the formaldehyde in the formalin introduced into the evolution vessel was, during the reaction, actually expelled from the formalin as formaldehyde gas, and absorbed by the water in the apparatus.

The Permanganate Formalin Method

As a method of fumigation, this seems first to have been proposed by Johnson, perhaps in 1902. The records of the Sioux Valley Medical Association, Sioux City, were destroyed by fire in 1905, and records of Johnson's statements were lost. There is no doubt that in December, 1903, Dr. Young called H. D. Evans' "attention to the fact that a mixture of potassium permanganate and formalin is attended by the formation of considerable heat, and the liberation of a gas which seemed to be formaldehyde." [12] In 1904 Evans and Russell worked on the chemical and bacteriological aspects of this method; the chemical experiments were not successful, the bacteriological results were excellent. In their last paper, Evans and Russell state, "When it had been shown that the method could be used successfully it developed that the method was first suggested in 1902-3, but it was given no publicity until 1904, when it was described in a paper by Dr. G. A. Johnson, of Sioux City, Iowa; the paper being read before the Sioux Valley Medical Association.[13]

The mixing ratio recommended by Evans and Russell at first was 187.2 grams permanganate to 500 cc. formalin. In a second paper, they changed this to 237.5 grams to 500 cc. The State Board

[12] Evans & Russell, 13th Rep., *loc. cit.*, p. 235.
[13] *Ibid.*, 14th Rep., p. 231.

of Health of Maine (1904) adopted [14] this mixing ratio, directing at the same time a formalin dosage of 500 cc. per 1000 cubic feet. It should be noted that nearly all American methods fall short of this State of Maine standard. Perhaps a false sense of economy is responsible for this.

Evans in his attempts apparently gained no exact knowledge of the chemical efficiencies at these ratios, but Base following him in time was able to arrive at definite results for the weight of formaldehyde actually in the air of a "zinc-lined room" fumigated with permanganate-formalin mixtures. Base changed the mixing ratio to 250 grams per 500 cc., because it "gave a residue fairly free from liquid." [15] Base was interested in the chemical results and in his experiments used a formalin dosage of 300 cc., McClintic was conducting the bacteriological investigations that ran along with Base's experiments, and McClintic raised the formalin dosage to 500 cc.[16] The percentage by volume of formaldehyde attained by following McClintic is 0.21 per cent., while that attained by following the State Board of Health of Maine is 0.20 per cent.; Horn found the chemical efficiencies to be 37.4 per cent. and 35.6 per cent. respectively.

In 1915 Hasseltine reduced the formalin dosage to "10 ozs." [17] using 5 ounces permanganate; the effect of these changes was to lower the concentration to 0.12 per cent. by volume and, as we shall show later, to reduce the available water below the safe limit. Under the directions given by Hasseltine, the bacteriological results must be regarded as uncertain.

William H. Park in his recent book gives two variations of the permanganate-formalin method (without data and without references). According to him, "Satisfactory results have been obtained from the following combination of chemicals; 2 ounces of quick-slaking coarsely granular lime (calcium oxide); 5 ounces of permanganate of potash; ½ gm. oxalic acid; 5 ounces formalin (40 per cent. strength); 2½ ounces of water. This is sufficient in quantity to disinfect 1000 cubic feet of space in five hours. It is used as follows: The lime and permanganate of potash are mixed together.

[14] *Ibid.*, 14th Rep. p. 248.
[15] Base, *J. Amer. Chem. Soc.*, XXVIII, p. 975, 1906.
[16] McClintic, *Hygienic Bulletin*, 27, U. S. Pub. H. Service.
[17] Hasseltine, *Public Health Reports*, XXX, p. 2049, 1915.

. . . Over this is poured the freshly prepared mixture of formalin, oxalic acid and water. . . ." [18]

The chemist will naturally raise questions regarding Park's mixture that might not be raised by sanitarians. Why add alkali (lime) which hastens the oxidation in a process that is already so rapid that health officers have difficulty getting out of the room and getting the door sealed before the reaction of the permanganate upon the formalin is under way? Why follow the alkali (lime) by an acid (oxalic), when acids neutralize alkalis, unless enough of acid and alkali be used to gain by the heat of neutralization? Why add either oxalic acid or lime that you are later going to remove largely from the field of action through conversion into insoluble calcium oxalate? Why add an additinal reducing agent (oxalic acid) when you really plan the reduction to be brought about by the excess of formaldehyde you have provided expressly for that purpose? Why put needlessly the burden of measuring or weighing lime, oxalic acid, and water, and of mixing them properly, upon "the laborer" who does the actual fumigating? Experience shows it is very hard to get the simplest fumigation procedures practiced properly every time. Why add water when it is well known that, other things being equal, water usually lowers the yield of formaldehyde?

We subjected Park's suggestion to experiment. It seemed to us wise to start with nothing but permanganate and formalin, in the mixing ratio given by Park; this may be called *the control*. We then ran a second set of assays, and in these we included the lime. In a third set we further added the water and in a fourth set we completed Park's formula by using also the oxalic acid. In order to avoid misunderstanding, the following table (Table V), is given setting forth the quantities of chemicals we used in this series of experiments.

TABLE V

Series	$KMnO_4$ gr.	Formalin cc.	Lime gr.	Water cc.	Oxalic acid gr.
I (control)	2.39	2.5			
II	2.39	2.5	0.95		
III	2.39	2.5	0.95	1.25	
IV	2.39	2.5	0.95	1.25	0.0085

[18] Park, *loc. cit.*, p. 234.

The results of these experiments follow (in Table VI):

TABLE VI

Chemical Efficiencies

Series I Control	Series II	Series III	Series IV
55.4%	54.7%	43.8%	46.0%
54.7	54.0	43.0	44.5
	55.4	44.5	43.8
		45.2	46.0
			43.8
			44.5
			43.0
			44.5
Average			
55.1	54.7	44.1	44.5

These experiments lead to the conclusion that William H. Park has given directions that waste time, labor, and chemicals; and that the "satisfactory results" reported by Park could have been gotten more economically and more rationally by using solely permanganate and formalin.

Park states, "Another combination is: lime 2.7 ounces, potassium permanganate 5.5 ounces; formalin 7.4 ounces, water 2.7 ounces. . . ." Here we note the water is less, in proportion to both the lime and the formalin. Upon assaying this mixture, we obtained the following results:

46.0%
44.5
44.5

Average 45.0% by vol.

In round numbers, permanganate and formalin alone if used in the same proportion without any lime or added water would yield 44 per cent. (as calculated from earlier results by one of us). Therefore it seems fair to say that there is no gain by following the directions given by Park, for one could use the permanganate and formalin alone just as effectively, without Park's addition of lime and water. By so doing, one would save time, labor, lime and water.

The Dichromate-Formalin Method

The use of a dichromate as the oxidizing agent in formalin fumigations was first suggested by Evans,[19] but he offered no experiments and there is no evidence that he ever tried it. Many years afterward Dr. Samuel G. Dixon and co-workers, without reference to Evans, and therefore perhaps quite independently, put forward a formula using sodium dichromate and formalin acidified with sulphuric acid. Later, to retard the polymerization that sulphuric acid hastens in formalin, glycerine was added to the formula. Dr. Dixon offered no experimental evidence upon the yield of formaldehyde by his procedure. One of us assayed this method and showed that it is of low efficiency and gives a concentration of only 0.07 volume per cent. of formaldehyde in the air of the room. The Pennsylvania Department of Health no longer advises fumigation, and this method has never found its way generally into the books on hygiene and public health. It has been sufficiently discussed by one of us elsewhere, and the data for the relation between mixing ratio and chemical efficiency is available in that place.[20]

The Lime-Formalin Method

Walker (1905)[21] described this method first as used by the Brooklyn Department of Health, but gave no record of any assay of it. McClintic reports[22] for it an efficiency of 14 per cent., and Walker calls for a dosage of 600 cc. formalin (in a mixture with aluminum sulphate and water). This would make possible a percentage by volume in a fumigated room of only 0.03. In 1907 Huber and Bickel[23] omitted the aluminum sulphate, increased the formalin dosage to about three times that of Walker, used four times as much lime and three times as much water, boiling hot. MacNutt[24] retained the dosage used by Walker but increased the lime. None of these modifications seems to have been tested quantitatively.

Park describes the "Lime and Formalin Method" as follows: "To 10 ounces of 40 per cent. formalin slowly add one ounce of concentrated sulphuric acid; pour this solution on to 2 pounds of quick-

[19] *Loc. cit.*, 13th Report, p. 236.
[20] Horn, *loc. cit.*, p. 41.
[21] *J. Amer. Chem. Soc.*, XXVII, p. 277, 1905.
[22] McClintic, *loc. cit.*, p. 63.
[23] *Münchener Med. Wochenschr.*, 1907, p. 1783.
[24] "Manual for Health Officers," New York, 1915, p. 581.

lime that has previously been broken into small lumps. . . . The liberation of a large amount of gas in a short time more than compensates for the loss by polymerization. A saturated solution of aluminum sulphate may be used instead of concentrated sulphuric acid." [25] The inference seems warranted that it would make little difference whether one used concentrated sulphuric acid or a saturated solution of aluminum sulphate. The use of concentrated sulphuric acid would certainly be avoided if possible because of its very destructive effects; its addition to the formalin long in advance of the time the mixture is used is not permissible because the acid hastens quite extensive polymerization of the dissolved aldehyde.[26] We were quite surprised, upon assaying these two procedures described by Park, to find that it does make quite a great difference indeed whether one uses concentrated sulphuric acid or uses a saturated solution of aluminum sulphate. Our results are given in the following table (Table VII).

TABLE VII

Chemical Efficiencies
Lime-Formalin Method
Park's Procedures

	With sulphuric acid	With saturated aluminum sulphate
	21.1%	16.3%
	21.5	15.5
	22.2	15.1
		15.5
Average	21.6	15.6

With the dosage given by Park, the percentages by volume of formaldehyde obtainable by these procedures are found to be 0.07 per cent. and 0.05 per cent. respectively.

The Bleach-Formalin Method

This method was introduced by Horn (1915) as a measure of economy when permanganate reached war prices. Its chemical efficiency at different mixing ratios was worked out and the original

[25] Park, *loc. cit.*, p. 235.
[26] Horn, *loc. cit.*, p. 43.

directions call for a formalin dosage sufficient to yield the same volume per cent. of formaldehyde in the air of the room as was yielded by the State Board of Health of Maine method and by McClintic's directions. The bleach-formalin method was condemned roundly [27] by Hamilton of the Parke-Davis & Co. Research Laboratories, but it was possible to show conclusively that Hamilton did not really know what he was talking about and had been misled by the faulty character of his own experiments.[28] The chemical efficiency of this method is 23.3 per cent. and the volume per cent. of formaldehyde in the air of the room is 0.21 per cent.

Faced with the same difficulty and desiring economy, the District of Columbia Health Department through Pozen and Dieter, printed [29] in 1919 a comparison of several proposed methods and fixed upon Horn's bleach-formalin method "as the most practical method, of those studied, for routine disinfection of rooms." But Pozen and Dieter decided to cut down the dosage of formalin from 800 cc. to 480 cc. Thus they simultaneously reduced the volume per cent. in the air of the room, from 0.21 per cent. to 0.13 per cent. Even after this, they state that, "in spite of this reduction (in dosage) . . . it was efficient as a germicidal agent."

In a table (Table II) earlier in this paper we give the per cent. by volume of formaldehyde in the air of the room for all the methods we know of. In working up these data we took up Pozen and Dieter's results gotten by drawing air from fumigated rooms through water and determining the quantity of formaldehyde by the cyanide method. In looking critically into their figures, we were struck first by the low yields found by Pozen and Dieter, second by the fact that the order of the methods as to yield could not be confirmed by us, and third by a peculiarly exact relation of "multiple proportions" between the yields by the different methods. This exact multiple relation we are forced to regard as exceptional. We submit (in Table VIII) Pozen and Dieter's results recast to show this relation and leave final judgment with the reader:

[27] "Facts and Fallacies in Disinfection," *Amer. J. Pub. Health*, VII, p. 282, 1917.

[28] Horn, *loc. cit.*, p. 39 and ff.; also *J. Ind. and Eng. Chem.*, XI, p. 126, 1919.

[29] *J. Ind. and Eng. Chem.*, XI, p. 448, 1919.

TABLE VIII

Pozen and Dieter's Reported Yields

I Method	II HCO.H(Gms.) per cu. ft.	III Calculated ratio of each yield give by P & D to yield by the lime method (given by P & D) taken as unity.
Permanganate	0.0221	3.250
Dichromate	0.0102 0.0102	1.500
Barium peroxide	0.0170	2.500
	0.0136	2.000
Chlorinated lime	0.0153	2.250
	0.0204	3.000
Sodium chlorate	0.0136 0.0136	2.000
Lime	0.0068 0.0068	1.000

We wish to make ourselves clear. The first and second columns above are taken directly from Pozen and Dieter's paper. The third column above gives the figures we get when we divide each of Pozen and Dieter's figures in the second column by their own last figure in the second column, namely, by .0068. We used a four place log table and obtained the values exactly as given in column III, *even to the third decimal place*. Such exactly simple relations among quantitative analytical results are unusual.

As previously stated we are unable to reconcile Pozen and Dieter's results with our own, when the various methods are arranged in order. Beginning (in Table IX) with the one yielding the largest volume percentage of formaldehyde and ending with the one yielding least, Pozen and Dieter's data lead to an entirely different arrangement from ours. This Pozen and Dieter arrangement our experiments show to be quite wrong.

TABLE IX

Order According to Decreasing Volume Per Cent.

Pozen and Dieter	Horn and Osol
1. $KMnO_4$	1. $NaClO_3$
2. Bleach (unmodified)	2. $KMnO_4$ Bleach (unmodified)
3. BaO_2	3. $Na_2Cr_2O_7$
4. $NaClO_3$	4. BaO_2
5. $Na_2Cr_2O_7$	

As their assays were all made by drawing air out of fumigated rooms and as all rooms leak more or less, we can readily understand how some errors may have crept in.

Rosenau's directions [30] for the bleach-formalin procedure do not conform to those given by Horn when the method was originally put forward by Horn. As Rosenau makes no mention in text or footnotes of any previous work on bleach formalin, the casual reader of his text book would probably be justified in taking the bleach-formalin method as an invention for which Rosenau should be held responsible. In the cases of the permanganate method and the barium peroxide method, Rosenau shows that he is not in the position of responsibility by naming the author or giving suitable references to the literature.

When Rosenau's directions for the bleach-formalin procedure are read in the light of what had been established previously by others, it appears that it is a modification of Horn's method and that it is a modification capable of yielding only 0.10 per cent. by volume of formaldehyde in the air of the room, whereas the directions Rosenau gives for the permanganate-formalin method yields 0.21 per cent. by volume. It is paradoxical for Rosenau to give without stated reason a new formula for the bleach method along with an old formula for the permanganate method when his new formula for Horn's bleach method does not yield even approximately the same volume per cent. of formaldehyde as the other, and when Horn's original directions yield exactly the same volume per cent. as the permanganate method Rosenau describes.

Assuming that this matter had been reasoned out, it would seem to follow that Rosenau thought the formaldehyde generated by bleach was $\frac{21}{10}$ or 2.1 times as germicidal as formaldehyde generated by permanganate.

As if in substantiation of this relation, we may use a statement of Rosenau's to the effect that the gas evolved from formalin by the bleach contains 3 per cent. chlorine.[31] This statement of Rosenau's is interesting, if true. Horn had shown that the gases *en masse* passed over moist litmus paper do not bleach the litmus; and that the total precipitate with neutral silver nitrate (which therefore in-

[30] Rosenau, *loc. cit.*, p. 1375.

[31] *Ibid.*, p. 1373.

cluded carbonate also) was of the same order of magnitude as the experimental error.[32] It might be urged that neither of these are conclusive proofs of low content of chlorine gas, but this inconclusiveness is today readily made good by adding orthotolidine to the absorption water used in the assay. We have used orthotolidine on the absorption water and find only minute quantities of chlorine; such as, 1.5 parts per million in 600 cc. of absorption water. Rosenau's statement is: "In the case of bleaching powder only about 3 per cent. of the total gas set free is chlorine." We do not know the *total gas set free,* but we do know the total formaldehyde set free. We also know that water vapor is set free along with formaldehyde, and we know Evans' and Russell's experience that oxidation of formaldehyde in fumigations yielded carbon dioxide and other gases as well. Therefore we are sure that when we reckon the chlorine found by orthotolidine back on the formaldehyde *alone,* we must arrive at a percentage that is of necessity higher than the true percentage of chlorine in the "total gas set free," whatever that may be.

When we thus calculate the percentage of chlorine in the formaldehyde we know to be set free, we find less than 0.08 per cent. (less than eight one-hundredths of 1 per cent.) and therefore we know that Rosenau's statement quoted above is a statement that is not true.

Rosenau further adds water, not contemplated in Horn's method, to make in advance a paste with the chlorinated lime. Chlorinated limes do differ markedly in dryness. At the time (1915) when the bleach-formalin method was devised the exceedingly dry chlorinated limes were less common than today. Also the standard for chlorine content was on the average higher; the U. S. P. standard called for not less than 30 per cent. active chlorine whereas chlorinated limes today frequently bear the legend "active constituents 24 per cent."

Very dry chlorinated limes do not wet up promptly; but we have no knowledge of any case where the reaction failed to occur sooner or later. With the dryest limes we have used, it has required ten minutes or more for the reaction to start. Presumably it is this dryness that Rosenau sought to obviate by adding water enough to form a paste, for (as will be shown later) Horn's bleach-formalin

[32] Horn, *Proc. Del. Co. Inst. Sci.,* 1920, p. 35; *Journ. Ind. and Eng. Chem.,* XI, p. 126, 1919.

mixture per se already contains more available water than any other fumigation mixture ever proposed. Upon the basis of assays we find no ground for objection to this addition of water beyond the fact that it is a needless added complication. When the action does not begin inconveniently soon the very dry finely pulverent limes we find can be mixed to a paste with the formalin itself. As Pozen and Dieter stated: "This factor (manipulation) must be considered because the laborers who do the practical disinfecting may not take the requisite care to insure efficient disinfection. For that reason the simplest efficient method should be chosen. . . . The chlorinated lime method (Horn's) is recommended for routine disinfection as combining germicidal efficiency, economy, and simplicity of manipulation."

In the following table we give our results on the assay of Rosenau's proposal and a re-assay with materials from the same stock, of Horn's method. The bleach used was found to contain 31.5 per cent. available chlorine.

TABLE X

Chemical Efficiencies of Lime-Formalin Method

Horn's method	Rosenau's modification
16.3%	23.3%
23.3	22.6
23.3	23.0
16.0	23.3
24.1	21.1
19.2	23.0
19.0	21.5
24.1	17.0
16.3	21.1
	19.0
Average 20.2%	Average 21.5%

We conclude that Rosenau has added nothing by his modifications of the bleach method but has reduced the factor of safety in germicidal action by lowering the dosage of formalin and has introduced a complication into the practical manipulation of the method.

At the same time Rosenau has left a trap for the unsuspecting whereby they will fall into the error that Hamilton of the Parke, Davis & Co. Research Laboratory ignorantly and boastfully flaunted years ago as one of his "Facts and Fallacies," namely the erroneous belief that large amounts of chlorine gas are given off in the bleach-formalin procedure. *The chlorine given off in bleach-formalin fumigations amounts only to some hundredths of a per cent. by volume of the formaldehyde simultaneously set free.* Our experiments with ortho-tolidine we interpret as follows: Since the maximum chlorine found is 0.80 per cent. of the formaldehyde evolved, and since the formaldehyde evolved is 0.21 per cent. of the air of the room, then it follows that the maximum concentration of chlorine to be expected in the air of a room fumigated by Horn's bleach-formalin method amounts to 0.000168 per cent. (by volume) of the air of the room.

The Barium Peroxide-Formalin Method

Crandall, Medical Director, U. S. Navy, briefly proposed [33] the pouring of formalin upon barium peroxide, as a more economical procedure at that time (1917) than the use of permanganate. Crandall must be presumed to have satisfied himself in some way regarding this method for he states, "The method outlined above on repeated trials gave gratifying results and showed conclusively that *barium dioxide is in all respects as efficient as potassium permanganate for liberating formaldehyde and water vapor from formalin.*"

We have italicized the part of Crandall's statement that experiment shows conclusively is not true. The results of our assays of Crandall's method follows:

No. 1	17.5%
No. 2	19.0
No. 3	18.2
No. 4	17.5
Average	18.1%

We quote Horn's findings [34] for the efficiency of mixtures of permanganate and formalin in Table XI.

[33] Crandall, *U. S. Navy Medical Bulletin*, XI, p. 519, 1917.
[34] Horn, *loc. cit.*, p. 38.

TABLE XI

Mixing ratio	Chemical efficiency
1000	70.9
730	56.4
500[38]	52.7
250[37]	37.4
237[36]	35.6
187.5[35]	30.1
150	22.4
100	10.5

All mixing ratios that we know to have been recommended by anyone are marked by footnotes. The lowest efficiency for permanganate is 30.1 per cent. (against Crandall's 18.1 per cent.), and this was with the lowest used mixing ratio—a ratio first used by Evans and Russell but abandoned by them within a year for a higher mixing ratio. Crandall's "method outlined above" has an efficiency of 18.1 per cent., or $\frac{18.1}{30.1} = 0.60$, as great an efficiency as the permanganate method at its worst and $\frac{18.1}{37.4} = 0.48$, or less than half the efficiency of the usual permanganate method. Experiment thus clearly contradicts Crandall's positive statement and unequivocally shows that barium dioxide is not nearly "as efficient as potassium permanganate. . . ."

With a chemical efficiency of 18.1 per cent., and the use of one pint of formalin we calculate Crandall's procedure could yield about 0.10 per cent. by volume of formaldehyde gas in the air of the room.

The Chlorate-Formalin Method

This procedure was devised in 1911 by Storm.[39] No mixing ratio and no charge of formalin per 1000 cubic feet was suggested by Storm. He left that to "those who may be interested in the prac-

[35] Evans & Russell.

[36] Evans & Russell.

[37] McClintic.

[38] The highest mixing ratio in the literature does not reach 500. Park in the procedure using lime, permanganate, water and oxalic acid, uses the highest mixing ratio for permanganate, namely, 479.

[39] Storm, *J. Ind. and Eng. Chem.*, X, p. 123, 1918.

tical side of the question." Storm showed that 25 grams of (sodium) chlorate to 100 cc. of formalin gave "the best results, that is, . . . there is practically no liquid left in the residue . . ." The only investigators who have left a record regarding the "practical side" of Storm's procedure seem to be Pozen and Dieter; they used a mixing ratio of approximately 1.77 grams to 5 cc., instead of the proportion that Storm states gives the best results; they used one pint of formalin per 1000 cubic feet.

We have assayed Storm's method using his mixing ratio (1.25 grams $KClO_3$ to 5 cc.) with the following results:

	54.7%
	56.2
	56.2
	55.4
Average	55.6%

This by itself might be a misleading figure, for it must be remembered that Storm's method involves the necessity of heating the reaction mixture in order to start the reaction. We accomplished this in our assays by using hot water (at 80° to 85° C.) as absorption water. In order to determine how much of the formaldehyde evolved might be due to this mere heating without any chemical action, we introduced into our apparatus the same volume of formalin without any chlorate whatsoever and allowed it to stand the full three hours. Our results on "controls" run in this way were:

	21.9%
	24.1
	24.1
Average	23.4%

In so far as it is fair to regard these as control runs, it seems also fair to conclude that the corrected chemical efficiency of Storm's method is 55.6 per cent. (total) minus 23.4 per cent. (due to external heating) = 32.2 per cent., due to heat from chemical action.[40] If a

[40] The much feared chlorine need not be dreaded in Storm's method any more than in Horn's method. We find by experiment that in both methods the total quantity of substances that might be taken for chlorine is less than the experimental error in titration in the Volhardt-Romijn method for determining formaldehyde. *Cf.* Horn, *loc. cit.*, p. 35.

pint of formalin be used per 1000 cubic feet (following Pozen and Dieter) and this mixing ratio just experimented with be preserved, it is clear that Storm's method will yield 0.30 volume per cent.; and this is more than by any other method we know of. If Storm were interested in the practical side of his method, he could develop it, we think, into a very useful form; as it stands, it will likely never come into general use.

Formaldehyde and Room Temperature

Evans first proved that the formaldehyde gas found by analysis to be actually present in the air of a room falls off rapidly with the temperature of the room, when other known factors are kept constant. We find within the limits of Evans' experiments that this functional dependence may be fairly well stated by the linear equation:

$$y = \tfrac{3}{4}\,x - 24, \qquad \text{in which}$$

y = the per cent. of total formaldehyde found by analysis in the air of the room,

x = temperature of room (degrees Fahrenheit).

The following table (Table XII) and graph (Figure 4) give Evans' results, and the percentages calculated by the equation just given:

TABLE XII

x Temperature F of the room	% Formaldehyde evolved as found by Evans	y % Formaldehyde calculated from our equation	Differences %
55°	16.8	17.2	+ .4
64°	24.1	24.0	— .1
74°	32.5	31.5	—1.0
80°	33.9	36.0	+2.1
83°	36.2	38.2	+2.0

These results of Evans seem to suggest the probability that other things being constant the volume per cent. of formaldehyde is a linear function of the temperature.

Humidity in the Room

The general equation we formulated for the germicidal effect indicates that in a satisfactory fumigation the germicidal action is

a function of the humidity, when all the other variables are kept constant. The best knowledge to date seems to be summed up in the following rule: "If the temperature is below 65° F., or if the relative humidity is below 60 per cent., the results become irregular; much below these figures the results are unreliable, especially if the space is both cold and dry." [41] This generalization is an oft-repeated one,

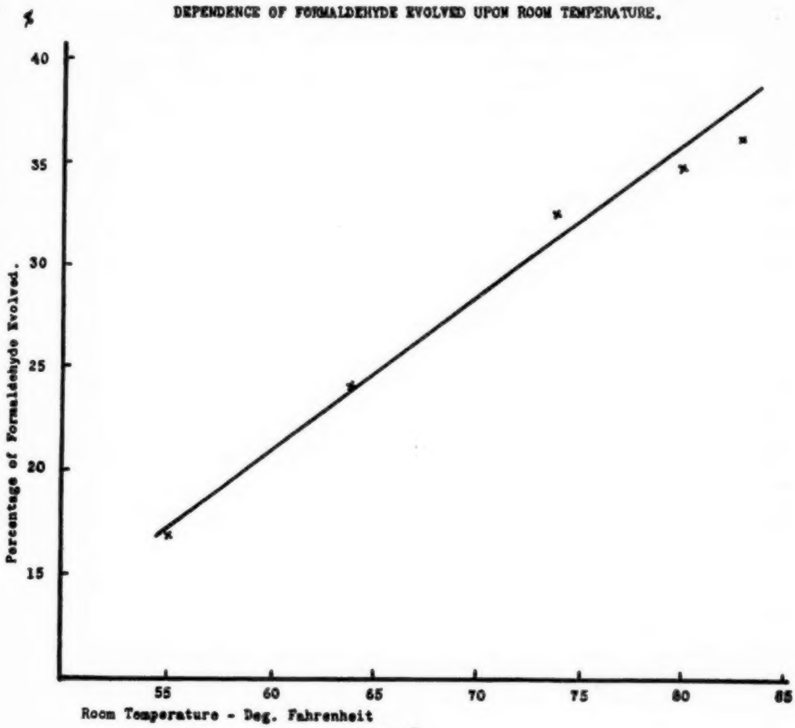


FIG. 4

and finds a place in most text books of hygiene. Many have violated this simple rule.

It is not hard to calculate how much water must be available from a fumigation mixture in order to meet this rule. In the following table (Table XIII) we give the pounds of water needed per 1000 cubic feet of air space in order to give a final relative humidity of 60 per cent., starting with an initial relative humidity of 35 per cent. These values appear in the fourth column of the table.

[41] Rosenau, *loc. cit.*, p. 1372.

TABLE XIII

Legend of Table: First column, temperature on dry bulb; second column, pounds water needed per 1000 cubic feet to give 35 per cent. relative humidity; third column, pounds water needed per 1000 cubic feet to give 60 per cent. relative humidity; fourth column, pounds water that must be supplied by fumigation mixture in case original humidity is 35 per cent., so that 60 per cent. may be finally realized.

Abscissæ on graph	Curve IX 35% on graph	Curve III 60% on graph	Difference, Lbs. water still needed per 1000 cu. ft.
100	.998	1.711	.713
99	.970	1.663	.693
98	.942	1.616	.674
97	.916	1.570	.654
96	.890	1.526	.636
95	.864	1.481	.617
94	.839	1.439	.600
93	.815	1.397	.582
92	.792	1.357	.565
91	.768	1.317	.549
90	.746	1.278	.532
89	.723	1.240	.517
88	.703	1.204	.501
87	.681	1.169	.488
86	.661	1.133	.472
85	.641	1.099	.458
84	.622	1.066	.444
83	.603	1.033	.430
82	.585	1.002	.417
81	.566	.971	.405
80	.550	.943	.393
79	.533	.913	.380
78	.517	.886	.369
77	.501	.860	.359
76	.486	.834	.348
75	.471	.808	.337
74	.456	.782	.326
73	.442	.758	.316
72	.428	.735	.307

Abscissæ on graph	Curve IX 35% on graph	Curve III 60% on graph	Difference, Lbs. water still needed per 1000 cu. ft.
71	.415	.712	.297
70	.402	.689	.287
69	.389	.667	.278
68	.377	.646	.269
67	.365	.626	.261
66	.353	.606	.252
65	.342	.586	.244

These data are also shown by graph in Figure 6. The first column of the table gives the abscissae, the second column along with the first gives curve IX, the third column along with the first gives curve III, and the fourth column can be read from the graph as the differences in the corresponding ordinates of curves III and IX.

Given these data (especially the fourth column in Table XIII) along with a knowledge of the average per cent. of water in formalin, elementary reasoning leads one to the minimum volumes of formalin it is safe to take for each 1000 cubic feet of air space. By the rule cited, volumes of formalin less than these minima can only be expected to yield results that are "irregular" or "unreliable," whenever the original relative humidity in the room before fumigation is much below 60 per cent. In other words volumes of formalin less than these leave no margin of safety. The following table (Table XIV) sets forth these minimum volumes of formalin calculated for four different temperatures by aid of Table XIII; values for any other temperature between 65° and 100° F. can easily be found.

Table XIV

Temperature	Minimum volume of Formalin
65° F.	195 cc.
75°	269 cc.
85°	366 cc.
95°	493 cc.

It would seem to follow that all methods for fumigation that recommend or direct less than 500 cc. (round numbers) of formalin for each 1000 cubic feet are "unreliable" per se—because they do

not contain enough water to insure germicidal humidity at all room-temperatures even if all of the water is vaporized (which, it seems, it seldom is). This is true regardless of the formaldehyde these mixtures simultaneously yield. By this reasoning the following methods become classed as "unreliable" or "irregular" in their germicidal action because of insufficient available water:

Hasseltine—U. S. Public Health Service.[17]
Park I—Permanganate, formalin, water, lime and oxalic acid.[8]
Park II—Permanganate, formalin, water and lime.[8]
Hasseltine—N. Y. Department of Health.[17]
Park III—Lime and alum.[8]
Park IV—Lime and sulphuric acid.[8]

As illustrating more fully this conclusion and the potentially misleading character of any method laid down without due regard to humidity, we have selected the New York City method of fumigation (as given by Hasseltine [17]). In Table XV we have given data showing just how great must be the initial relative humidity in any room *before* fumigation by this New York City method, in order that *after* fumigation by this method the final relative humidity shall equal the necessary minimum of 60 per cent. relative humidity called for by the rule as a prerequisite for regular and reliable germicidal action.

TABLE XV

Degrees F. Dry Bulb	Lbs. H_2O needed per 1000 cu. ft. to give 60% relative humidity	Lbs. H_2O furnished (maximum) by N. Y. Method given by Hasseltine	Lbs. H_2O needed in air of room before fumigation in order that after fumigation there may be 60% relative humidity	Necessary initial relative humidity in room if 60% is finally to be realized
65	0.59	0.24	0.35	36%
66	0.61	0.24	0.37	37
67	0.63	0.24	0.39	38
68	0.65	0.24	0.41	38
69	0.67	0.24	0.43	39
70	0.69	0.24	0.45	39
71	0.71	0.24	0.47	40
72	0.73	0.24	0.49	40

Degrees F. Dry Bulb	Lbs. H_2O needed per 1000 cu. ft. to give 60% relative humidity	Lbs. H_2O furnished (maximum) by N. Y. method given by Hasseltine	Lbs. H_2O needed in air of room before fumigation in order that after fumigation there may be 60% relative humidity	Necessary initial relative humidity in room if 60% is finally to be realized
73	0.76	0.24	0.52	41
74	0.78	0.24	0.54	41
75	0.81	0.24	0.57	42
76	0.83	0.24	0.59	42
77	0.86	0.24	0.62	43
78	0.89	0.24	0.65	44
79	0.91	0.24	0.67	44
80	0.94	0.24	0.70	45
81	0.97	0.24	0.73	45
82	1.00	0.24	0.76	46
83	1.03	0.24	0.79	46
84	1.07	0.24	0.83	47
85	1.10	0.24	0.86	47
86	1.13	0.24	0.89	48
87	1.17	0.24	0.93	48
88	1.20	0.24	0.96	48
89	1.24	0.24	1.00	50
90	1.28	0.24	1.04	50
91	1.32	0.24	1.08	50
92	1.36	0.24	1.12	50
93	1.40	0.24	1.16	50
94	1.44	0.24	1.20	50+
95	1.48	0.24	1.24	50+
96	1.53	0.24	1.29	51
97	1.57	0.24	1.33	51
98	1.62	0.24	1.38	51
99	1.66	0.24	1.42	51
100	1.71	0.24	1.47	51

In the graph (Figure 5) the curve shows how this initial prerequisite varies with the temperature. If one will look over the weather bureau records for relative humidity in any city, and then

study this curve, he will come to a full realization of how the germicidal results by this New York City method must often have been "irregular" and "unreliable." It will then be very clear that to base any conclusion regarding the uselessness of terminal fumigation upon the morbidity reports of a city using this method, amounts merely

NEW YORK CITY METHOD OF FUMIGATION.

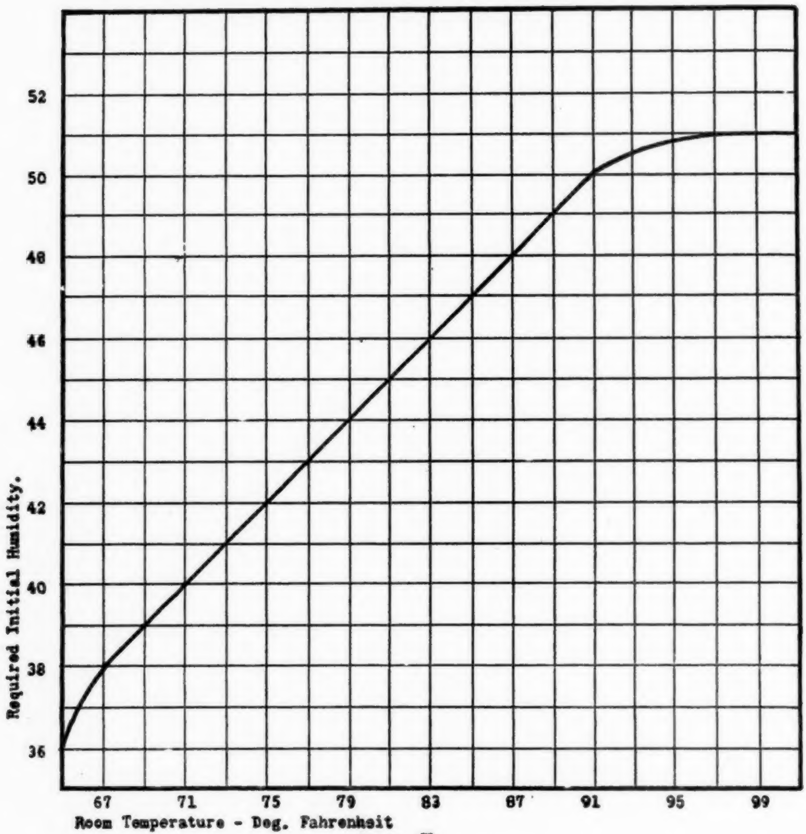


FIG 5

to deceiving one's self and misleading others. Such reasoning is an abuse of statistics and of the confidence of those who are easily convinced.

The obvious thing to do when there is danger of insufficient humidity, is to add water to the formalin. Unfortunately almost

always the effect of added water is to cut down the yield of formaldehyde. This is of course known only to those who have gone back to the literature of fumigation but it is a fact that cannot be disputed in the larger number of instances. Horn showed [42] that this decrease in chemical efficiency is concomitant with a decrease in the maximum temperature attained in the reaction mixture in the instances of the permanganate and the bleach methods.

It may be urged, on behalf of those who thus appear to have recommended methods that can only reasonably be expected to yield "irregular" and "unreliable" results, that additional water is produced in all those methods where an oxidizing agent acts. It is true that both formaldehyde and methyl alcohol yield water upon oxidation. In the following table (Table XVI) the water (stated in pounds) present as such originally in the quantity of formalin recommended per 1000 cubic feet is called the "solvent water." This is done to distinguish it from the calculated yield of "water by oxidation." In the calculation it has been assumed that one molecule of water results from the oxidation of each molecule of formaldehyde or of methyl alcohol.

TABLE XVI

Pounds of Water Available in Several Methods

Author	Park	Hasseltine	Park	Hasseltine	McClintic	Horn
Description	I	N. Y. Dept.	II	U.S.P.H.S.	U.S.P.H.S.	
Solvent water	0.19	0.20	0.28	0.37	0.63	1.00
Water by oxidation	0.06	0.02	0.10	0.14	0.23	.44
Theoretically available water	0.25	0.22	0.38	0.51	0.86	1.44

The situation with respect to these several methods of fumigation is shown graphically in Figure 6. The points at which the graph for any method, cuts the graph (plotted from data in Table XIII) for 60 per cent. relative humidity shows the limiting temperature beyond which the method fails to meet the rule even *when every point is stretched in its favor.*

In Figure 6, the heavy faced curve marked III on the right-hand margin shows (as ordinates), the pounds of water needed in 1000 cubic feet of air to give 60 per cent. relative humidity at any of the temperatures (shown as abscissæ). Curve IX shows the pounds of water needed to give 35 per cent. relative humidity. Taking 35

[42] Horn, *loc. cit.*, p. 26.

per cent. relative humidity as a reasonable minimum in the air of most cities in this country, we have added to the ordinates of IX the pounds of water calculated for the several methods of fumigation given in Table XVI. This gives a family of parallel curves each showing for some one method the maximum pounds of water in 1000 cubic feet fumigated by that method (assuming enough water present initially

DEPENDENCE OF WATER NEEDED, UPON ROOM TEMPERATURE.

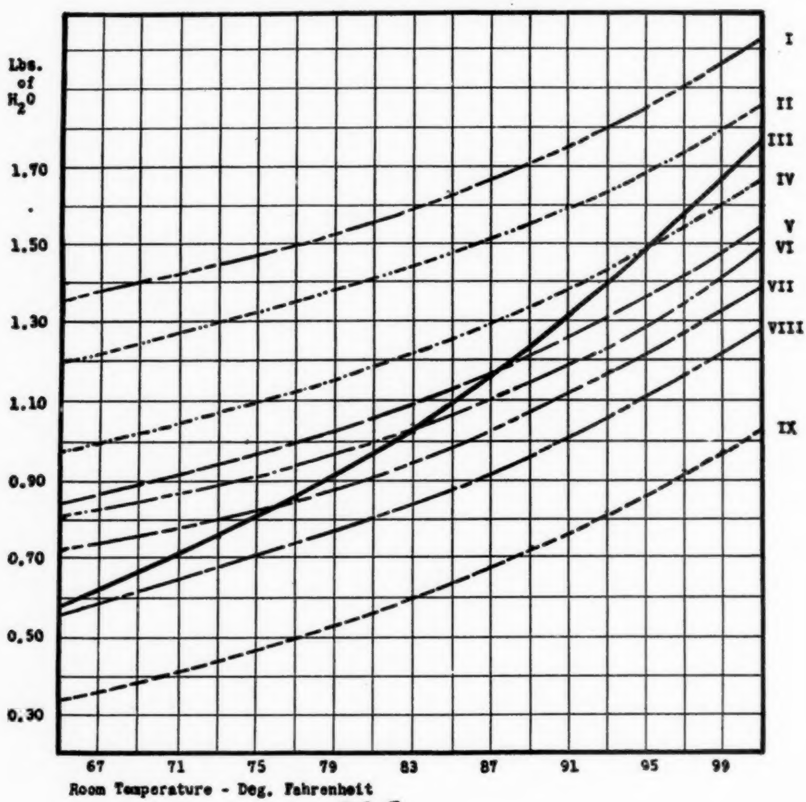


FIG. 6.

and before fumigation to give 35 per cent. relative humidity in this 1000 cubic feet). This family of parallel curves present data for the following methods, respectively:

VIII. The New York City method as given by Hasseltine.
VII. Park's "B" method.
VI. Hasseltine's suggestion of 300 cc. dosage.

V. Hasseltine's suggestion plus water of oxidation.
IV. Base's suggestion without water of oxidation.
II. McClintic's method.
I. Horn's bleach-formalin method.

It becomes evident from an inspection of Figure 6 that the following conclusions may be drawn concerning the maximum humidity attainable in each of the several methods of fumigation, provided the relative humidity in the room before fumigation is 35 per cent.

1. Using the New York City method as given by Hasseltine (Curve VIII) the relative humidity in the air of the room during fumigation (within the range of ordinary temperatures), is always less than the accepted standard of 60 per cent.

2. Park's "B" method (Curve VII) cannot meet the humidity requirement when used at temperatures above 76° F., even though all the water is vaporized.

3. Insofar as humidity requirement is concerned, Hasseltine's suggested 300 cc. dosage (Curve VI) eliminates the possibility of using the method at temperatures above 83° F. (water of oxidation not being included in the water which is available).

4. Upon adding the water which might be produced by oxidation when using Hasseltine's suggested 300 cc. dosage method, the humidity "safe limit" is raised to 88° F. (Curve V).

5. The maximum water available in Base's suggestion for fumigation (Curve IV), (but not including water of oxidation), is sufficient to produce at least a 60 per cent. relative humidity at temperatures up to 95° F., provided all the water is vaporized.

6. McClintic's method (Curve II) is within the 60 per cent. "safe limit" for all ordinary room temperatures.

7. Horn's method of fumigation (Curve I) has more water available than any of the other methods considered.

It would be incorrect to think of this discussion as theoretical. Not only is there no question that so much and only so much water exists in formalin, and that so much and only so much additional water could be formed in the oxidation, but it is also true that independent bacteriological experiment (apparently free from all consideration of water vapor), has demonstrated that when the volume of formalin per 1000 cubic feet is reduced below 500 cc. a value is soon reached at which the germicidal action becomes uncertain. Evans

and Russell, and later McClintic, followed this reduction in extensive bacteriological studies. The State Department of Health of Maine was not just *guessing* when it adopted 500 cc. of formalin as the official quantity per 1000 cubic feet; this quantity was adopted by them "in order to give a satisfactory margin of safety." It has been an error for any one entering this field with a new method to neglect a careful study of the subject. Everyone who trifles with the subject of fumigation finds it a farce; and this is not surprising, for the trifler usually first makes a farce out of it.

Duration of a Fumigation

This is a point upon which there is no general agreement. We know of no directions however lying outside of the limits of five to twenty-four hours. It is of course a matter upon which there should be some general agreement, and therefore a matter best settled by some representative committee of dependable men.

Resistance to Formaldehyde

This matter seems mostly to have been left to others to investigate. McClintic distinguished clearly between the greater resistance of the tubercle bacillus as compared with other pathogens. Park offers the statement, "The necessary concentration of gas in the surrounding atmosphere varies with each species of micro-organisms," and we wonder if he knows this as the result of direct experiment or has merely inferred it from the fact that different species of micro-organisms are different.

Should Terminal Fumigation Be Abandoned?

Whenever this question has been answered, yes, or no, it has been answered not upon knowledge but upon opinion. Recently those who are opposed to the practice have found satisfaction in the extensive statistics of Chagas,[43] which bear testimony that in South America it has made little or no difference in the contagious disease *rates* to drop fumigation. There have been much less extensive but equally convincing data of the same kind available in the United States for several decades. Opposed to this are the unquestionable evidence (1) that most proponents of methods of fumigation have

[43] Office International d' Hygiène Publique, Bulletin Mensuel; Tome XVIII, pp. 484-520, 1926.

taken no pains to make their proposals conform to the best knowledge and standards to date, and (2) that most of the fumigations have been made by these methods in a perfunctory way and without reference to scientific aspects of the matter. Whenever by chance an operator used an efficient method under circumstances (of temperature, humidity, etc.), which at that time by chance favored germicidal action, that test by experience would be reliable; but we think it must be admitted that probabilities have frequently been against such favorable fortuity. Assuming the problem to be simple, assuming it to involve only methods and practice, such data as Chagas' though massive do not lead unequivocally to the conclusion some have inferred, namely that all terminal fumigations are useless. Chagas' data, and other of the same kind, show equally well the results of any one or more of four things: (1) the good practice of bad procedures; (2) the bad practice of good procedures; (3) the bad practice of bad procedures; or (4) the good practice of good procedures. The fourth is the most improbable of all; and yet unless it obtains throughout, the data fail logically to show the sanitary futility of terminal fumigations.

Further, assuming to be true what is ordinarily contrary to fact, namely, that Chagas' and similar data represent the results of the good practice of good methods, the situation involves other important considerations. Only a fraction of the total contagious diseases ever reach the records of health boards; the Hagerstown experiment leads one to expect about four out of five cases of contagious disease to escape official notice, so there is always ample opportunity for secondary infections. If infection is by way of environment, elsewhere than in the environment fumigated, the chances of arresting reinfection by perfect terminal fumigation are not great. Just how many reinfections occur by personal avenues (warm breath, spray, discharges, etc.) to every one reinfection by way of environment we cannot guess with any degree of satisfaction.

The persistence of pathogens in environment for greater or less lengths of time is a fact of observation not to be pushed lightly aside; but evidence as to the virulence of pathogens after such exposures to unfavorable conditions is meager. Some take the view that there is no danger of reinfections from environment; to all such, even perfect fumigation is useless. Although environment is less important than personal contact, it remains a factor of unknown weight in the dissemination of disease.

So far as we know all who have advocated the abandonment of fumigation have recommended "chemical cleansings" of all surfaces in the environment. Chapin says that his hopes that the abandonment of fumigation would lead to greater cleanliness have not been realized. If the extreme view be taken that there are no virulent pathogens in the environment, then it is idle to cleanse the surfaces "chemically" or in any other way—unless it be for æsthetic reasons. Those who have given thought to chemical cleansing of *all* surfaces know that it cannot be done.

There are at least two courses with respect to terminal fumigations open to sanitarians today. One of these is to admit frankly that the problem is full of difficulties and the procedures full of contradictions and that, since nobody knows how much or how little good proper terminal fumigation may have done, terminal fumigations should be abandoned. This amounts to saying, "We give it up." The other course is to turn the matter over to a suitably selected committee, as of the American Public Health Association or of the American Medical Association, to "debunk" it, to standardize the procedure so as to insure its germicidal power and to give thus to fumigation the opportunity to accomplish whatever good it can. In the gross, it may well be as potent a factor in prophylaxis as some of the more obvious procedures, such as quarantine in the instance of several diseases. We are not sure if we were to do away with quarantine in whooping cough, for example, there would be any observable change in the *gross* figures for that disease any more than there is an observable change in *gross* figures where terminal fumigation has been abandoned. Our experiments clearly show that there are fumigations and fumigations. We selected whooping cough as our example since, although its mortality is usually higher than that of scarlet fever, it is admitted that it "has not been given the study its importance deserves" and that "much of our knowledge is assumed." We hold no brief for or against fumigation, but we are convinced by the experimental data we have presented that the matter need not be discussed or dismissed in a manner unworthy of scientific men. The right or wrong of fumigation is within grasp, but the hand that reaches toward it should be guided by "knowledge" and not by "opinion."

MICROCHEMICAL ANALYSIS

By Henry Leffmann

THE APPLICATION of the microscope to the detection of minute amounts of substances is coeval with its invention. In the *"Arcana Naturæ"* of Antonio Leeuwenhoek, published in 1696, numerous excellent drawings are given, the product of careful and skillful studies with the instrument, with the invention of which he was so largely concerned. I append to this essay a copy of a drawing of crystals, which may be regarded as the earliest example of microchemical analysis. Much later, Sertürner in his discussion of the so-called "morphine controversy," furnished to Gilbert's *Annalen* in 1817 (55, 89 and plate II) a drawing made by himself of "morphine salt," and a drawing of "opium salt" that Derosne had prepared. The beginning of the dispute as to the discovery of morphine goes back to the first luster of the nineteenth century. Derosne, being a Frenchman, is quoted at that time as "Citizen Derosne," a form that recalls the Terror and, to many, Defarge and the wine shop in San Antoine.

The microscope is now indispensable in the chemical laboratory. Inventive talent has greatly multiplied its efficiency and range of application. It has been widely applied for many years in chemical analysis. One of the most striking instances of systematic employment in such work was by Dr. Theodore G. Wormley, who, in 1869, published a comprehensive treatise entitled "Microchemistry of Poisons" illustrated with many excellent steel engravings of crystalline forms of the more familiar poisons, largely, of course, precipitates obtained by action of special reagents on solutions thereof. The alkaloids are especially in evidence. Wormley, however, was not content with simple qualitative precipitations. He used exact proportions, and thus not only showed the characteristic forms but gave accurately the limits of delicacy. The following extract from Dr. Wormley's book will show his method of presenting data: (The test was made with a salt of morphine and sodium hydroxide).

"1/100 of a grain of morphine (as sulphate) in 1 grain of water yielded with a small drop of the reagent, after a few moments, a crystalline precipitate, which in a little time increased to a copious deposit." The precipitate is figured in an engraving on Plate IV, figure 6. Wormley also found that 1/1000 of a grain could be detected by careful manipulation.

The application of photography to microchemical analysis was a great step forward. It is not possible here to review the history of this method, but a very considerable advance in technic was made in the late 60's of the last century by Dr. Joseph J. Woodward, U. S. A., then attached to the office of the Surgeon General at Washington. Woodward's work was carried on actively for several years and resulted in great improvements in the methods of photomicrography, especially in the construction of objectives. In recent years great attention has been given to all phases of photographic reproduction of the field of the microscope and the technic has been brought to a high degree of efficiency. Instruments to aid in drawing from the field are available and an extensive literature has developed.

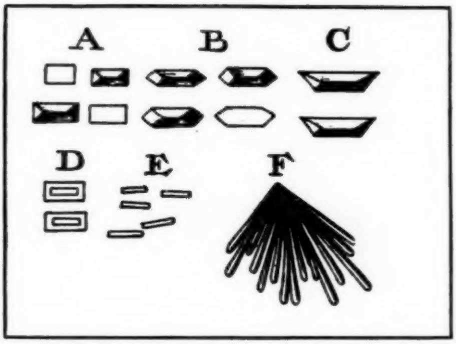
It seems to me that exaggerated importance is being given to the economy of the methods of microchemical analysis. In the great majority of cases, the materials subjected to test are cheap and fairly abundant, so that the fact that only minute amounts may be used is really of little moment. The principal advantage of the application of photography to microchemical analysis is that a permanent record of the microscope field can be made. The plan of producing crystals on the slide under a cover glass, restricts development of the form, it limiting it largely to two dimensions. Crystals should form slowly and should be allowed opportunity to develop in three dimensions. Mineralogists, who are the most intensive students of crystallography, point out that such phrases as "needles," "brushes," "dendritic forms," have no definite value. Needles may be combinations of prisms or other forms. Better results can in many cases be obtained by producing the crystals in small amount in a test-tube and placing a few of them on the slide. Often the mount can be examined without cover glass. For all such purposes a vertical arrangement is best. A field that needs further exploiting is the use of polarized light. This in many cases produces brilliant and characteristic colors. Very extensive application of this is made in mineralogy, highly complicated accessory apparatus being employed, an outfit much too costly for the ordinary pharmacologic laboratory.

Drawings and photographs have only moderate value in teaching the practical applications of microchemical analysis. The student and the expert worker should rely on actual observation. For exercise, a student may be required to make drawings, care being taken that this is really done from the field and not from a book.

In all cases, the magnification should be stated. Indications by titles of oculars and objectives are not sufficiently informing. As a

rule, low powers should be used. Greater depth of focus is obtained and crystals show more solidity.

Operation with known and pure materials is of little practical value. It is equivalent to giving a student in qualitative inorganic analysis a sample of copper sulphate with request to detect the copper. That is not the problem in actual laboratory work. It is to detect several metals in the presence of each other, indicating them definitely and precisely. For the research pharmacologist and the toxicologist,



Copy (natural size) of an illustration in Antonio Leeuwenhoek's *Arcana Naturae,* published in 1696. The book is in the library of the College of Physicians of Philadelphia. The drawing, presumably on wood or copperplate, is probably the earliest delineation of a microscope field.

the problem is exemplified by examining a mixture of powdered cinnamon, nux vomica and coffee, detecting and distinguishing accurately cinnamic aldehyde, strychnine and caffeine.

Henry Leffmann Chemistry Research Fund.
Wagner Free Institute of Science.

A PROPOSED THIOSULPHATE NUMBER FOR OLIVE OIL

By Wallace H. Dickhart

THIS ARTICLE is written for the sole purpose of suggesting the possibility of a new characteristic for olive oil. It is a modification of a test proposed in 1923. See "The Detection of Olive Oil in Some Refined Vegetable Oils," by W. H. Dickhart.*

*The American Journal of Pharmacy, 1923, p. 684.

Reagents

From past experiments the following method was decided upon: Solution "A." Pour slowly one part of concentrated sulphuric acid into four parts of dehydrated alcohol, placing the graduate in cold water if necessary to reduce the temperature.

Solution "B." A 2 per cent. alcoholic solution of furfurol. It has been suggested that this solution be made from freshly redistilled furfurol. It is advisable to make solutions "A" and "B" as needed.

Solution "C." Tenth normal sodium thiosulphate, the same solution that is used to determine iodine value.

Solution "D." Carbon tetrachloride.

Modification

Weigh into a four-ounce oil bottle 7.05 grams of olive oil, add from an accurate pipette 5 cc. of Solution "A," shake, and then cork if more than one sample is to be tested. Place the bottle in boiling water (100° C.) for three minutes, shaking lightly each minute. When the bottle is placed in the boiling water it will reduce the temperature for a few seconds. Start the time from the reboiling point. After three minutes remove the bottle and add 10 cc. of cold water to the mixture, shake and cool the bottle, either under tap water or in a beaker of cold water. When the mixture is at room temperature add 5 cc. of carbon tetrachloride, and titrate with tenth normal thiosulphate solution with vigorous agitation until it is of the same milky color as the blank which should be run at the same time, using either corn or cottonseed oil.

The reason for selecting 7.05 grams of oil as a unit is because a sample of oil can be weighed at the same time for two different determinations, one for the free fatty acid, and the other for the thiosulphate number.

Experimental Data

	Thio No.	Iodine No.	Val. Index	Coin Test	F.F.A.
Marked Virg. Oil	3.69 cc.	86.3	1.4629	Negative	0.45%
" " "	4.28 "	82.7	1.4635	"	0.40%
" " "	4.48 "	86.5	1.4620	"	0.50%
" Pulp Ref. Deo.	3.23 "	87.0	1.4620	Positive	0.45%
" French Ref.	3.90 "	87.4	1.4630	Negative	0.48%
" Rapeseed	0.00 "	104.3	1.4675	"	0.50%

	Thio No.	Iodine No.	Val. Index	Coin Test	F.F.A.
(10% Olive Oil and 90% Rapeseed Oil)	1.59 cc.	102.9	1.4670	Negative	
(90% Olive Oil and 10% Rapeseed Oil)	4.78 "	87.1	1.4640	"	
Unknown Olive Oil	5.28 "[1]	84.8	1.4630	"	0.70%
" " "	3.48 "	82.4	1.4630	"	0.50%
" " "	5.48 "	84.6	1.4632	Positive	0.40%
" " "	6.18 "	87.9	1.4623	"	3.40%

Proposed Thio Numbers

Recently a sample of oil marked olive oil gave a thio number of 1.59. The iodine value was determined and found to be 134.0. This unknown indicated that the thio number could be used to detect olive oil in a mixture from 5 to 10 per cent. in other oils.

It would seem that from the above figures the limits for a virgin oil would run from 4 to 4.5 thiosulphate number, for refined deodorized oils from 3.50 to 4.00, and for untreated bleached foots oil from 5 to 6. These numbers are arbitrary and are only a suggestion for experimental work.

The chart shows very little difference in the index except with the rapeseed and the mixture of 90 per cent. rapeseed and 10 per cent. olive oil.

The iodine values all come within the limits of the U. S. P.,[2] except the rapeseed and the 90 per cent. rapeseed mixture. Presumably the thio numbers would indicate that olive oil above 4.50 and below 3.50 should be investigated to determine the purity of the oil.

It has been found recently by another chemist that olive oil gave a pink or red color, pecan oil and grape fruit seed oil a pale pink, whereas cottonseed, sunflower, soya bean, linseed and china seed oils did not give a pink or red color with the above reagents.

If sesame oil is present in the olive oil the red color will appear in the cold, and then there is no need to obtain the thio number.

When an olive oil contains oil of rosemary, it should be extracted with alcohol to remove the essential oil.

[1] The thio number of the olive oil used in the rapeseed oil mixture.
[2] *United States Pharmacopœia*, tenth revision.

CHEMICAL CHARACTERIZATION OF DRUGS

By L. Rosenthaler

Communication from the Pharmaceutic Institute of the University of Berne

MICROCHEMICAL TESTS for mucus in mucous drugs: The only reaction, which is mentioned in the 6th edition of the German Pharmacopœia of a test for mucus in mucous drugs is found under *radix althœae* and reads: Powdered *radix althœae* is characterized by mucous cells and by small balls of mucus formed by crushing these cells.

To test the mucus in the official Malvaceæ drugs, its property of precipitating with ferric salts may be used, as I have pointed out (*Ber. Deutsche Pharm. Gesell.*, 31, 27, 1927). The sliced drug is placed in ferric chloride solution, washed thoroughly, may even be placed under the faucet, then put into a solution of potassium ferrocyanide. The mucus becomes dark blue. The powdered drug is best shaken in a small test tube with ferric chloride, then filtered through a small filter, washed thoroughly and a little bit placed on a cover glass in a solution of potassium ferrocyanide.

Another method is the following: The material is placed for about five minutes in a perfectly clear lead acetate solution, then washed with distilled water free from carbon dioxide and then placed in a solution of potassium-dichromate. The mucus assumes a yellow color. In both methods, other elements besides the mucus are colored, but this does not in any way interfere with the test.

Both reactions may be used with other herbs, the Prussian blue reaction may be used in the case of *Semen Lini*, the lead chromate reaction in the case of *Tubera Salep* and *Bulbus Scillæ.* If slices of the last mentioned drug are placed in a 10 per cent. tannin solution, one can see in every cell round or irregularly shaped clots of various size. Very often in one cell only one clot is formed. These formations are mainly of mucus and tannin, for the following reasons: 1. The mucus of *bulbus scillæ* is flocculated by tannin as many other slimes. 2. These clots are still formed, if the sliced drug is boiled with alcohol, but not if it is extracted with water. 3. Besides the clots, no coagulated mucus can be observed.

On the other hand, it should be mentioned, that similar structures are formed not only with tannin but with iodine-potassium

iodide solution, also with the sliced drug extracted with alcohol. However, the substance precipitated by iodine is identical with mucus. For if *bulbus scillæ* is first extracted with alcohol and then with boiling water, then filtered, the filtrate gives with tannin a strong precipitate, while with iodine potassium iodide no precipitation occurred.

To test the mucus in slices and in powder form of Tubera Salep, alkaline copper solution, which colors the mucus blue, is suitable. Occasionally, not regularly, however, I have noticed that after twenty-four hours the center of the mucus cells remained red through the cuprous oxide formed, while the outer zone remained blue. In contrast to the colorless cell membranes a very beautiful picture was obtained. According to W. Peyer (*Jahresber. der Caesar & Loretz* A. G. 1926) it is important to bear in mind that the mucus of *tubera salep* differs with varying age and origin.

On a Microchemical Test of Some Cations in nonorganized Drugs

Although many substances can be tested directly microchemically, it is important to point out, that a negative test is not always a proof that even simple reactions can be prevented by the presence of other substances. I have not been able for instance to test for potassium in *pulpa tamarindi,* although there is no doubt that it is present and I have obtained a positive test for potassium in the ash of the bark of the *tama,* when the direct test gave negative results. This test will of course also fail, if the quantity of the substance tested is very minute.

The microchemical experiments, which I am about to describe here and which all have been carried out on cover glasses were worked out for potassium, sodium, and magnesium. The following reagents were used: for potassium, copper lead nitrite, for sodium uranyl-acetate, for calcium, iodic acid and for magnesium Pfahl's mixture of phosphates. Of all of these the potassium test alone is not entirely reliable, as ammonium gives the same reaction. The reaction of potassium was only obtained with gum arabic, the presence of potassium was definitely established in the ash of it. In testing for ammonia a solution of potassium hydroxide was placed in a washing bottle, to which 5 gm. of gum arabic were added. Air was passed through, and then through a bottle containing dilute hydrochloric acid. The content of the last washing bottle gave after the addition of potassium hydroxide and Nessler reagent a positive reaction, particularly in the case of Senegal Gum.

The following substances were investigated: Agar, Aloe, (Capensis, Barbados, Natal), Ammoniacum, Asafœtida, Catechu, Euphorbium, Galbanum, Gambir, Gum arabicum, Gutti, Kino, Kirschgummi, Manna, Myrrha, Sarcocolla, Sterculia-Gummi, Tragacanth.

Positive tests were not obtained with all samples of Opium investigated, but the aqueous extraction did give all positive tests. Kino did not always give positive tests. In the case of Gutti the test was only obtained with the aqueous solution, in the case of succus liquiritiæ, only two of the six investigated samples proved positive.

The test for magnesium was positive with all samples investigated; also with Agar, Ammoniacum, Catechu, Euphorbium, with Galbanum, partly very weak. Kino, cherry gum, Myrrha, Sterculia-Gum Succus Liquiritiæ and Tragacanth. In the case of Asafœtida and Gutti not every sample showed a positive reaction.

No positive test for sodium was obtained in any of the samples tested for it.

In quantitative respect, very great differences were observed and it may be mentioned that with the varying composition of the substances a uniformity of the above described reactions canot be expected.

Chemical Characterization of Herba Lobeliae

Herba Lobelia is one of the drugs for which the 6th edition of the German Pharmacopœia specifies no chemical test. I have, therefore, undertaken a few experiments.

The aqueous extract prepared by heat (1:10) gives with ferric chloride a dirty brown precipitate, besides turbidity with some of the alkaloid-precipitating agents (iodine-potassium iodide in the presence of hydrochloric acid, bromine-potassium bromide, Mayers reagent). As these reactions are absolutely non-specific, I decided to utilize the fact, reported by H. Wieland, C. v. Schoepf and W. Hermenn, that *Lobeliæ* is decomposed by acids and alkalies under formation of volatile aromatic compounds.

If 5 gm. of Lobelia are distilled with 50 gm. of water and 5 gm. of sodium hydroxide, so that 10 cc. of the distillate are collected, it will give the following reactions:

Sodium nitroprusside and sodium hydroxide produce a deep orange to dark purple color, which on the addition of acetic acid turns purple violet and then dirty violet. With phenylhydrazin hy-

drochloride or with 1-4 nitrophenylhydrazin (in dilute acetic acid) immediately a strong turbidity is formed. The distillate obtained without sodium hydroxide does not give the characteristic reaction with sodium nitroprusside and will give only very faint turbidities with the two hydrazins. Controls of this reaction were carried out with *Folia Belladonnæ, Coca, Jaborandi, Stramonii,* and *Uvae Ursi.* With or without sodium hydroxide the distillate did not show the above described reactions.

ABSTRACTED AND REPRINTED ARTICLES

TRANSPARENT EMULSIONS OF SOME ESSENTIAL OILS[1,2]*

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THE EMPLOYMENT of essential oils as flavors has attained an important position in many of our modern food industries. These oils may be used either straight, in alcoholic solution, or in the form of an emulsion, which is a dispersion of the oil in minute globules in some liquid medium. Emulsions consisting of essential oils dispersed in concentrated aqueous sugar solution have been found well adapted for flavoring fondants, gum goods, and confectionery products composed largely of sugars. By employing a dispersion medium that is miscible in all proportions with the material to be flavored, it is possible to get a uniform distribution of flavor throughout the entire batch.

The subject of flavor emulsions is by no means new, but there is still room for considerable improvement and development in this field. Some types of emulsions are unstable preparations of oil in

[1] Received April 15, 1929. Presented before the Division of Agricultural and Food Chemistry at the Seventy-seventh Meeting of the American Chemical Society, Columbus, Ohio, April 29 to May 3, 1929.

[2] This paper is based upon a thesis presented by Richard E. Linehan in partial fulfilment of the requirements for the degree of bachelor of science in chemistry at the Polytechnic Institute of Brooklyn.

*Reprinted from *Journal of Industrial and Engineering Chemistry.*

water containing gum arabic or tragacanth as the peptizing agent. Their short duration of stability indicates the need of fuller application of the principles of emulsification in the manufacturing process. It is well known that the size of the dispersed globules has an important bearing upon the stability of an emulsion—the smaller the globules, the greater the duration of stability. When prepared by an ordinary shaking or stirring operation until the two phases are mixed intimately, an emulsion contains dispersed globules of comparatively large and variable diameters. Much superior dispersion may be obtained by the use of a high-speed colloid mill or homogenizer, which gives a much finer and a more uniform disperse phase than could be attained by simple agitation methods. Smaller particles present a larger total surface area for adsorption of the peptizing agent, exert less attractive force upon one another, and thus promote a greater degree of stability.

Besides an improvement in stability, it is highly desirable to produce transparent emulsions instead of the usual opaque variety, since a homogeneous-looking product is always more satisfactory than a translucent or opaque one. It is well known that by equalizing the refractive indices of the dispersed phase and the dispersion medium there is neither reflection or refraction of light, and a transparent emulsion or mixture results. In this study, employing a concentrated aqueous solution of invert sugar (or, as was subsequently found more satisfactory, two parts of invert sugar and one part of sucrose) as the dispersion medium, it was found possible to adjust its refractive index to that of the oil to be emulsified and thus obtain a transparent emulsion of the essential oil.

General Procedure

To study the problem of preparing stable transparent emulsions of essential oils, considerable work was performed, and this paper presents the results of the most successful experiments. The refractive index of the oil to be emulsified was determined at 25 degrees C. The dispersion medium was made up by dissolving the desired amount of peptizing agent in water to which was added a sufficient quantity of an 80 per cent. solution of invert sugar—or a mixture of two parts of invert sugar and one part of sucrose—to make the refractive index of the mixture equal to the refractive index of the oil. The oil was then added to the dispersion medium, well mixed, and the mixture

homogenized three times through the Hurrell homogenizer, a continuous type colloid mill, operating at 2850 rpm. In every instance the emulsion produced was transparent. A sample of the resulting emulsion was then centrifuged at 1750 rpm. for five minutes to test its stability. In order to consider sufficient the amount of peptizing agent employed, the emulsion was required to withstand this test without any indication of breaking. In working with small quantities, air was incorporated in the process of homogenization, but with large amounts of emulsion it was only necessary to feed the mixture continuously and keep the funnel of the homogenizer full to exclude the air. The inclusion of air is objectionable because it renders an emulsion temporarily opaque until the air is expelled either by rising of its own accord due to gravity or by centrifuging in the case of very viscous emulsions.

Efficiency of Various Peptizing Agents

A series of experiments was carried out to determine the relative efficiency of gum arabic, gelatin, agar-agar, and tragacanth as peptizing agents. For this purpose orange oil was selected as the disperse phase and the volume emulsified kept constant at 5 per cent. in each case. The amount of peptizing agent was gradually reduced until a concentration was reached at which the emulsion broke when centrifuged. The minimum amount of peptizing agent that would stabilize a 5 per cent. emulsion under these conditions was considered the liminal value of the peptizing agent for a 5 per cent. orange emulsion. As the table shows, gelatin proved to be the best of the peptizing agents investigated. A high-grade calfskin gelatin was employed. The liminal value was found to be the same (0.05 per cent.) for orange, peppermint, rose, and lemon oils, but the duration of stability with these oils varied. The effect of the concentration of peptizing agent upon the duration of stability was observed by retaining samples of the emulsions for daily observation. These data for 5 per cent. orange emulsion are given in the accompanying table.

Although gelatin proved to be an excellent peptizing agent, the emulsions began to grain, or deposit crystals, within two or three months, presenting an obstacle that had to be overcome before the emulsions could have any commercial value. The graining was due to crystallization of dextrose from the invert sugar constituting the dispersion medium. Experience with sugar products has shown

that this crystallization can be overcome by the use of a mixture of two parts of invert sugar and one part of sucrose, instead of straight invert sugar. Consequently, this mixture was tried in the preparation of these emulsions, and the result was satisfactory. Five per cent. emulsions made with the 2:1 mixture and 0.25 per cent. of gelatin have shown no indications of graining or breaking over a period of eleven months. Emulsion 60 in the table is an example.

Relative Efficiency of Various Peptizing Agents

Dispersed phase: Orange oil, 5 per cent. by volume, n_D at 25° C., 1.4690.
Dispersion medium: Invert sugar and water containing peptizing agent; n_D at 25° C., 1.4690.

No.	Peptizing Agent	Effect of Centrifuging	Duration of Stability	Other Observations
2	5% gum arabic	Stable	2 months	Grained slightly
36	2.5% gum arabic	Stable	7 weeks	Grained slightly
30	1% gum arabic	Stable	4 weeks	Grained heavily
4	0.5% gum arabic	Stable	3 weeks	Grained heavily
6	0.25% gum arabic	Broke	......	....
9	1% gelatin	Stable	3 months	Did not break, but grained
10	0.50% gelatin	Stable	3 months	Did not break, but grained
11	0.25% gelatin	Stable	3 months	Did not break, but grained
60*	0.25% gelatin	Stable	11 months	Began to grain after 11 months
12	0.10% gelatin	Stable	6 weeks	Broke, grained
13	0.05% gelatin	Stable	1 month	Broke, grained
14	0.025% gelatin	Broke	......	....
21	0.25% agar-agar	Stable	7 days	Grained in 3 months
25	0.10% agar-agar	Stable	6 days	Grained in 3 months
26	0.05% agar-agar	Stable	5 days	Grained in 3 months
27	0.025% agar-agar	Stable	3 days	Grained in 3 months
28	0.010% agar-agar	Broke	......	....
22	0.50% tragacanth	Stable	1 month	Difficult to homogenize; retained air; broke and grained.
23	0.25% tragacanth	Broke	......	....

*Graining retarded by employing a mixture of 2 parts of invert sugar and 1 part of sucrose instead of straight invert sugar.

Relation Between Amount of Dispersed Phase and Quantity of Gelatin Required as Peptizing Agent

In many instances an emulsion of high flavor concentration is desirable. Consequently, a number of experiments were made to determine the relationship between the dispersed phase, the peptizing agent, and the degree to which the dispersed phase may be increased from a practical viewpoint.

The emulsions were made up as outlined under General Procedure, employing orange oil as the dispersed phase and gelatin as the peptizing agent. Quantities of gelatin ranging from 0.25 to 1.00 per cent. were taken and the amount of orange oil successively increased until a concentration was reached at which emulsification was no longer complete.

With 0.25 per cent. of gelatin it was possible to incorporate 15 per cent. of orange oil in an emulsion; 0.50 per cent. of gelatin, 20 per cent. of orange oil; and 1.00 per cent. of gelatin, 30 per cent. of oil. When these concentrations were exceeded, emulsification was incomplete and there was a tendency for the emulsion to gelatinize and break. Best results were obtained by adding the oil to the dispersion medium in portions of 5 per cent. at a time and homogenizing after each addition of oil. As the concentration of the oil phase increased, the emulsions became more viscous and difficult to homogenize. The results of this part of the work indicate that the relationship between the amount of dispersed phase and the quantity of peptizing agent required for stability is not directly proportional, **but the ratio of peptizing** agent to dispersed phase increases as the concentration of the oil is increased.

Properties of Emulsions

In every instance the emulsions prepared in this investigation proved to be of the oil-in-water types. This was expected, since the peptizing agents employed were all water-soluble and oil-insoluble. Observations on viscosity and viscosity variations disclose that the viscosity of the emulsions varies with the nature and concentration of the peptizing agent employed, the concentration of the dispersed phase, and the percentage of sugar in the dispersion medium. An increase in any one or all of these factors will cause an increase

in the viscosity of the emulsion produced. In some cases, notably orange emulsions of high oil content, high viscosity was accompanied with prolonged stability. On the other hand, a 5 per cent. emulsion containing 0.05 per cent. of gelatin showed a higher viscosity than a 5 per cent. peppermint oil emulsion with the same amount of gelatin, but the peppermint emulsion retained stability twice as long as the orange emulsion. Furthermore, emulsions prepared with agar-agar or tragacanth as the peptizing agent were much more viscous than any in which gelatin or gum arabic was used, but the stability of the former was poor while that of the latter was good. These findings indicate that high viscosity alone does not cause emulsification or account for stability, but is a favorable factor when other conditions are right.

Stability Towards Temperature Change, Acids, and Alkalies

In order to determine the susceptibility of these emulsions to changes in temperature and acidity, a number of emulsions were subjected for four days to temperatures ranging from 0 degrees to 90 degrees C. Transparency was not much affected within a range of five degrees above or below 25 degrees C., at which temperature the refractive indices of the two phases were equalized, but below 20 degrees or above 30 degrees C. the emulsions gradually became opaque. The stability, however, was not affected over this temperature range, showing that the emulsions will stand up under any range of temperatures likely to be met in storage.

A number of samples were taken from the same orange emulsion, and to them were added 0.03 per cent. HCl, 0.05 per cent. HCl, 0.59 per cent. HCl, 0.05 per cent. NaOH, and 0.08 per cent. NaOH, respectively. The emulsions containing the alkali rapidly turned brown and broke down. The effect of the acid was not so pronounced, but when the samples began to break the rate of oil separation was proportional to the acidity. The conclusion deduced from these experiments is that a neutral or slightly acid medium is conducive to maximum stability of the emulsions. Alkali must be avoided, since sugars in alkaline solution oxidize rapidly with the formation of highly colored products. Furthermore, alkali tends to destroy the protective gelatin film around the dispersed oil particles.

Transparent Emulsions of Essential Oils of High Refractive Index

In the preparation of transparent emulsions of orange, peppermint, and rose oils, no difficulty was experienced in adjusting the refractive index of the dispersion medium so that it was equal to the refractive index of the oil under consideration. Furthermore, no trouble was experienced in passing the emulsions through the homogenizer, each one flowing freely and giving transparent emulsions of high quality. No such satisfactory results were attained in adjusting refractive indices when an attempt was made to prepare emulsions of wintergreen, anise, and cinnamon oils. The high refractive indices of these oils require invert sugar solutions of unattainable concentrations to produce transparent emulsions. In order to attain the high refractive index required for transparency, other dispersion mediums were tried. A 45 per cent. solution of sugar in glycerol was prepared by heating glycerol and sucrose to 130 degrees C. with 0.10 per cent. of tartaric acid, and this was tried as the dispersion medium. The refractive index of this solution was 1.4960 at 25 degrees C., but its viscosity was so high that it stopped the homogenizer when an attempt was made to prepare a wintergreen emulsion.

Since no satisfactory dispersion medium of high refractive index was obtained, it was decided to attempt to lower the refractive index of the oil phase by the addition of sufficient quantity of the ethyl esters of coconut oil, prepared by alcoholysis of coconut oil with ethyl alcohol. The essential oils and these esters are mutually soluble. By using a solution of one part of oil and two parts of ester it was possible to reduce the refractive indices of wintergreen, anise, and cinnamon oils low enough to permit the use of aqueous sugar solution of sufficiently low concentration to pass through the homogenizer without difficulty.

The results of this work have demonstrated that coconut oil ester is a satisfactory material for reducing the refractive index of any essential oil to a value low enough to permit the use of concentrated aqueous sugar solution as the dispersion medium. Emulsions so prepared were satisfactory from the viewpoint of transparency and stability, but developed a pronounced cocanut taste on standing. It is hoped that some other esters more permanent in character than those of coconut oil may serve the same purpose and not develop the objectionable taste on standing.

Recommendations

It is recommended to employ 0.25 per cent. of gelatin as the peptizing agent for emulsions up to 5 per cent. by volume, in order to insure a long period of stability. For higher concentrations of oil, the amounts of gelatin specified in this paper for concentrated orange oil emulsions should be used.

Preparation of terpeneless instead of straight oil emulsions is recommended in the case of oils of the terpene variety, such as orange, lemon and lime. Terpeneless emulsions retain their flavor quality almost indefinitely owing to the removal of the terpenes, which oxidize and produce objectionable taste and odor.

MEDICAL AND PHARMACEUTICAL NOTES

Pharmacological Actions of Phenylethanolamine—The diminished efficiency of ephedrine on repeated administration and its depressant action on the heart suggested the advisability of study of related and similarly acting drugs, with the hope of providing cheaper and more efficient substitutes.

A drug which can be synthesized cheaply is phenylethanolamine. In 1915, Hirose reported that this drug raises blood pressure and acts as a mydriatic in rabbits, but he did not study the mechanisms of these actions.

Maurice L. Tainter, of the Department of Pharmacology, Stanford University School of Medicine, reports the result of an extended study of its pharmacological actions.

The phenylethanolamine sulphate used was a pure, white product, in the form of glistening white flakes; melting point, 239 to 240 C. (uncorrected); it was readily soluble in water, and a concentration of 7 per cent. was the maximum obtainable without heating in normal saline solution. The compound was stable, no less of strength could be noticed in solutions several months old.

Injected intravenously in anesthetized rabbits, cats and dogs, phenylethanolamine caused prompt increases in blood pressure. Cats and dogs responded better than rabbits. Pigeons responded in a similar manner although requiring somewhat larger doses than mam-

mals. The drug had little effect on the circulation when given by routes other than the intravenous. Successive intravenous injections of fully effective doses did not lead to a progressive diminution of the circulatory action as is the case with ephedrine.

Results seem to show that phenylethanolamine stimulates the circulatory organs (heart and blood vessels) by direct muscular action.

Conclusions

1. The pharmacological actions of pure phenylethanolamine have been extensively investigated and compared with those of epinephrine, and also with those of tyramine and ephedrine, reported in the literature.

2. The important actions consisted of circulatory stimulation, mydriasis and shrinkage of the nasal mucosa and turbinates.

3. The circulatory stimulation was mainly of cardiac origin, as indicated by marked increases in rate and amplitude of the heart together with definite and well sustained increases in blood pressure and a variable action on blood vessels, either a weak vasoconstriction or a vasodilitation. The action in the nose is due to vasoconstriction from the high concentration of the drug.

4. The mydriasis occurred after both local application and systemic injection of phenylethanolamine, and appeared to be due to direct specific stimulation of the radial muscle.

5. The action on the intestine was variable, consisting mainly of inhibition, but partly also of stimulation; the excised uterus of different species was invariably stimulated even after sympathetic nerve paralysis; the respiration and the untreated and constricted bronchi were practically unaffected.

6. The results of analyses of the important actions in intact animals, including ergotoxinized and cocainized animals, and on excised organs, indicated that phenylethanolamine is musculotropic and not sympathomimetic, except in the intestine.

7. Thus, the actions of phenylethanolamine resembled those of tyramine and ephedrine, and they differed considerably from those of epinephrine.

8. The main therapeutic uses of phenylethanolamine would be, local application in the nose for shrinkage of the congested mucosa and turbinates, and on the eye as a mydriatic. Less might be expected from its use in the treatment of depressed circulation (shock,

hypotonic conditions, etc.); here it would have to be injected intravenously, but without apparent loss of action on repeated injection and without cardiac depression, as is the case with ephedrine. An anti-edemic action is also possible, as previously reported.

9. The systemic toxicity of phenylethanolamine was found to be relatively low, and the local irritant action practically negligible. Solutions of phenylethanolamine can be boiled and are stable; the drug can be cheaply synthesized.—Maurice L. Tainter, *The Journal of Pharmocology and Experimental Therapeutics,* May, 1929, page 29.

J. K. T.

PROPOSED DEFINITIONS OF FOODS—Tentative definitions of fruit juice, grape juice, and orange juice were drawn up by The Food Standards Committee at a recent meeting of the committee in Washington, announces W. S. Frisbie of the Food, Drug and Insecticide Administration, U. S. Department of Agriculture, chairman of the committee. Criticisms and suggestions regarding the proposed definitions and standards are now invited from food officials, consumers, the trade, and all other interested parties.

The definitions proposed are as follows:

FRUIT JUICES: are the clean, unfermented juices obtained from the first pressing of sound, mature, fresh fruits, or of their pulp, and correspond in name to the fruit from which they are obtained.

GRAPE JUICE is the unfermented, expressed juice of clean, sound, mature grapes. It is made by a single pressing of the fruit, with or without the aid of heat, and with or without the removal of insoluble matter.

ORANGE JUICE is the clean, unfermented juice, with or without portions of the pulp, obtained from the sound, mature fruit of the orange, *Citrus sinensis,*

(a) by reaming or burring the cut fruit,
(b) by pressing the pulp after removal of the peel, or
(c) by presing the whole fruit with subsequent removal of oil derived from the peel.

Communications regarding these proposed definitions should be addressed to A. S. Mitchell, secretary, Food Standards Committee, Food, Drug and Insecticide Administration, Department of Agriculture, Washington, D. C., to reach him not later than February 1.

S. U. P. 36 for Influenza—This drug which is a symmetrical urea (para-benzoyl-para-amino-benzoyl-amino-naphthol 3:6 sodium sulphonate) was used by the author, in the form of intramuscular injection, in forty-two cases during the influenza epidemic in the spring of the present year, 0.5 cm. (0.00005 Gm.) was given as an initial dose, and on the fourth day .75 cm. The only drugs given orally to any of the patients were 2.5 grams of calomel and a simple expectorant mixture. At the end of a fortnight it was found that the injected patients had an advantage over the non-injected ones. In the former cases the duration of the pyrexia and headache was halved and the duration of the muscular pain more than halved. The earlier the injection is given, the greater the benefit. The general results are that the early initial dose completely aborts the attack in nearly every case, and that therefore if the treatment be used in influenza epidemics on a wholesale scale and early enough it is the most valuable agent at present discovered for combating such epidemics. Treatment given at a later stage, providing that the attack has not existed for more than forty-eight hours, considerably shortens the duration of the disease.—R. M. Pearce (*B. M. J.*, 3589, 663, 1929). *Through Pharm. Jour.*

Discover Two New Vitamins—No less than two new vitamins have recently been discovered by English scientists. Katherine Hope Coward and her colleagues at the Laboratory of the Pharmaceutical Society here have just published a paper describing a new vitamin which has somehow escaped notice before. Scientists do not yet know whether this new factor is necessary for the human race, but Miss Coward's experiments have proved that it is necessary for the growth of that all-important animal, the experimental rat. No name has yet been given to this vitamin. It has been found in fresh milk, lettuce, grass, ox muscle, liver, and wheat embryo.

The other new vitamin has recently been described by Vera Reader of the Biochemical Department, Oxford University. The original Vitamin B was said to prevent beri-beri. Scientists found later that Vitamin B really consisted of at least two separate factors, and they decided to call them B1 and B2. Miss Reader now has found that in the Vitamin B of yeast there is a third growth factor which is chemically distinct from either of the other two. She suggested the name B3 for this new factor. Like B2, it can be destroyed by heat.

The Pellagra preventing factor in foodstuffs, known as P-P, was also once thought to be part of Vitamin B.—*Science Service.*

NEWS ITEMS AND PERSONAL NOTES

CHILEAN GOVERNMENT STUDIES PHARMACY OF IODINE—Pharmacists know that practically the only commercial source of iodine is the Chilean nitrate fields. These fields, as it is also generally known, are one of the principal sources of revenue of the Chilean Government. The Government, therefore, is interested in promoting and extending the use of all products and by-products of the nitrate fields.

Iodine is one of the most important of these.

The Mellon Institute of Pittsburgh has been appointed by the Government of Chile to carry on intensive scientific research in this field. In turn the Philadelphia College of Pharmacy and Science has been designated by the Mellon Institute to carry on investigations in the present and possible pharmaceutical uses of iodine.

The first investigation now under way at the Philadelphia College of Pharmacy of Science is intended to develop a practical means of retaining the well known antiseptic properties of iodine for local application in a vehicle which is less irritating than the present tincture of iodine. Linwood Tice, a graduate of the class of 1929, is the research fellow now engaged in this work under the immediate direction of Charles H. LaWall, Dean of Pharmacy.

PHOTOGRAPHY AT EASE—Photography is no longer an uncertain and troublesome hobby to those who are willing to adopt modern methods and materials. Many whose experience leads them to complain of disappointments and expense, will be agreeably surprised at the increased pleasure and decreased cost which follow the adoption of methods explained in a new booklet, "Photography at Ease," just published.

The booklet, which is well printed and illustrated with many pages in color, is concise, yet packed with up-to-date information. It tells, not only the procedure to follow, but also gives the reason. It leads the photographer from the moment of exposure, through the various stages, to the finished picture, at the same time finding space to discuss special subjects such as direct color work, panchromatism and color effects by toning, to name a few.

Every photographer will find much of interest in this booklet. The majority will appreciate its honest endeavor to smooth difficult paths, to make comfort in photographic manipulation a real thing and to point the way to the achievement of better results. The sections on exposure and development are of the utmost value to beginners. These sections tell how the light acts upon the plate or film and how the latent image is converted into a visible image, thus explaining the actual purpose of exposure and development.

"Photography at Ease" is a sensible booklet, serviceable to everyone interested in photogaphy. To any reader mentioning this paper, the booklet will be sent post free by the publishers: Burroughs Well-Come & Co. (U. S. A.) Inc., 9 and 11 East Forty-first Street, New York City.

THE ARTHRITIS PROBLEM—The late Sir William Osler is reported to have said that when he saw a chronic arthritic come up to his front door he felt inclined to jump out of the back window. In short, he recognized that the treatment of an arthritic patient is one of the most difficult problems with which the medical profession is faced.

And yet, to quote from the concluding words of Pemberton's latest work on the subject ("Arthritis & Rheumatoid Conditions," Lea & Febiger, Philadelphia), "there are few disease states for which more can be done."

Removal of infected foci, physio-therapy and analgesic measures all play an important part. Vaccines and foreign proteins are used by many physicians with good results. But, the arthritic is a human being, anxious to get well and to return to his daily work as quickly as possible. Often he cannot afford the time for protracted hospital treatment. Aspirin, iodides and other analgesic measures have to be taken in doses too large to allow him to "carry on." He feels a useless burden on the community.

With the advent of oxo-ate "b" (Calcium Ortho-Iodoxybenzoate) the arthritic is given a new chance of immediate usefulness and ultimate improvement. Oxo-ate "b" is a prompt analgesic and usually produces definite results such as decrease in swelling and muscle spasm, and an increase in the range of joint motion.

BOOK REVIEWS

DOWN THE WORLD'S MOST DANGEROUS RIVER. Clyde L. Eddy, formerly Editor of the *Druggists' Circular*. Published by Frederick A. Stokes Company, 443 Fourth Ave., New York City. Price, $2.50.

No one who had known this quiet young man, Mr. Eddy, by merely seeing him and coming into contact with him at pharmaceutical conventions, which he frequented by reason of his connection with a prominent drug journal, would have imagined that he had within him the adventurous spirit shown in this narrative. His persistence in undertaking the navigation of "the world's most dangerous river," the Colorado, in the face of all the testimony furnished by former expeditions, many of them disastrous, showed the spirit of the eternal boy which Mr. Eddy must possess. He and his twelve companions have given us an epic which in the reading produces many a thrill. Even though his crew consisted of young college men they proved to be no "toy soldiers" but played their parts like seasoned veterans. An expedition like this requires youth, enthusiasm, and a disregard for the minor creature comforts deemed so necessary later on in life, and this body of men seem to have possessed all of these qualities. Every page of the book is so filled with exciting happenings that there is no adequate way in which to describe it; the only way is to read it for one's self. Mr. Eddy's style is very readable and interesting and the book is very much worth one's while who cares for books of adventure, with the added interest that this tale is true.

M. R. L.

APPLIED PHARMACOLOGY. By A. J. Clark, M. C., M. D., F. R. C. P. Prof. of Materia Medica in The University of Edinburgh, 3d edition, 1929. P. Blakiston's Sons. Price $4.00.

We reviewed the first edition of this interesting book in 1923 (AMERICAN JOURNAL OF PHARMACY, 1923, p. 263). Since then the book has been considerably enlarged, the present edition being 529 pages as against 390 in the first edition.

The book is not a systematic treatise on either pharmacology or therapeutics. Its aim is to explain the clinical value of remedies on

the basis of our scientific knowledge concerning their actions; in other words to show the relations of laboratory pharmacology to clinical therapeutics. For any one who is interested in the idea of a rational therapeusis based on scienctific facts the book can be recommended. It makes, however, no claim to completeness and is not to be regarded as a reference book on any branch of pharmacology.

H. C. Wood, Jr.

The College of Pharmacy of the City of New York. A History. By Curt P. Wimmer, Pharm. D., A. M., Ph. M., Professor of Pharmacy. 10½ x 7½, 346 pages. Published in 1929.

Professor Wimmer might be expected to be in happiest vein when dedicating himself to a work such as he has produced here. It is a historical volume, published on the occasion of the one hundredth anniversary of the establishment of the College of Pharmacy of the City of New York.

So frequently historical compilations of this type assume hysterical complications—opinions and imaginings being paraded as facts.

In this work however, the author, has rigorously confined himself to facts, interestingly assembled—and has produced a volume, which is not merely a narrow record of the progress of the institution but a cross section of the history of pharmacy in the great State of New York.

Indeed one finds in it much of the history of early American pharmacy, for it was the East, and mostly New York and Boston and Philadelphia, that between them, carried the torch of pharmaceutic progress and carried it well, long before the rest of the country had dispensed with the business of local civilization. However, to the long line of alumni of the venerable institution, it is the College story that counts. Of its early history the author writes "conceived of necessity, born in humiliation, and passed through its periods of storm and stress, until after nearly fifty years of precarious existence, conditions arose in the profession of pharmacy which placed it (the college) upon a solid basis, enhanced its usefulness and caused it to take its place in the first ranks of the institutions of learning."

Today the College of Pharmacy of the City of New York boasts of a notable faculty—of a valued affiliation with the great Columbia—of a long list of some eight thousand alumni—surely a result that

has long since justified the spirit and courage of its founders and those who helped it through its days of storm and stress.

The format of the book is splendid, illustrations numerous and well-arranged. Indeed it is a work quite worthy of its distinguished author and of the institution that sponsored it.

IVOR GRIFFITH.